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Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing Escherichia coli in the Calgary Health Region: emergence of CTX-M-15-producing isolates. Antimicrob. Agents Chemother. 51: 1281-1286.

Pelczar JR, Harley JP, Klein DA (1993). Microbiology: Concepts and Applications. McGraw-Hill Inc., New York, pp. 591-603.

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*Full Length Research Paper*

# Knowledge of sexually transmitted Infections among patients attending outpatient clinics at University Teaching Hospital, Ado-Ekiti, Nigeria

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**The study was designed to assess the level of knowledge of sexually transmitted infections and possible factors associated with knowledge of patients attending outpatient clinic in University Teaching Hospital, Ado-Ekiti, Nigeria. This is to enable appropriate advocacy targeted on at risk population so as to control sexually transmitted infections and prevent its complications in this environment. A cross sectional descriptive study was carried out on patients attending outpatient clinics of the hospital from February to July, 2010. All volunteered participants were given a self-administered structured questionnaire. Out of the 592 interviewed, 242 (40.9%) were males and 350 (59.1%) were females. Although, knowledge of sexually transmitted infections was high in the general population, especially among those with postsecondary school education (85.4%) and the drivers (90.9%), it was relatively low among the adolescents and the youths who are the most vulnerable in this environment ($\chi 2 = 14.343$; $p < 0.05$). News media was the highest source of information about Sexually Transmitted Infections. Age, educational level and the type of occupation appear to be important factors affecting knowledge. Therefore, health education about Sexually transmitted infections targeted at this risk group may yield positive result.**

**Key words:** Sexually transmitted infections (STI), knowledge, Ekiti, Nigeria, youths and adolescents.

## INTRODUCTION

Sexually transmitted infections (STI) are spread primarily through person-to-person contact, although some of the pathogens that cause it, especially Human immunodeficiency virus (HIV) and syphilis, can be transmitted from mother to child during pregnancy and childbirth, and through blood products and tissue transfer (World Health Organization (WHO) Media centre, 2011; Nsuami et al., 2010). Sexually transmitted can be divided into those caused by bacteria, viruses and parasites (WHO media centre, 2011). STI are most common in young sexually active people. It has been reported that the incidence declines with age and that adolescents and young adults experience the highest risk of exposure to STI (Richard and Jay; 2002; Mudassir et al., 2010).

According to 1999 WHO estimates, 340 million new cases of curable STIs (*Syphilis, Gonorrhoea, Chlamydia and Trichomoniasis*) occur annually throughout the world in adults aged 15 to 49 years. In the developing countries, STI and their complications rank in the top five disease categories for which adult seek health care (WHO

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media centre, 2011). Some of these STI when not controlled can lead to severe complications. In men, gonorrhoea and *Chlamydia trachomatis* can lead to epididymitis. Inflammatory urethral stricture may arise later from poorly treated gonococcal urethritis, which in turn may lead to urinary retention and possibly chronic renal failure if not properly managed. Some of the diseases may result to genital ulcers, with few cases developing severe sacral dysfunction resulting in urinary retention (Richard and Jay, 2002; Gerald and Steven, 2002). Consequences of these STI include AIDS, spontaneous abortions, stillbirths, perinatal and neonatal morbidities, chronic pelvic pains, dyspareunia, infertility, increased risk of ectopic pregnancy and even death (Whitfield, 1986; De Schryver and Meheus,1990; Chamberlain, 1995; Westrom and Mardh, 1990; Rice, 1991; Robinson and Ridgeway, 1996; Otolorin, 1999).

Interestingly, STI are preventable diseases and their prevention is even a priority for World Health Organisation (WHO) (WHO media centre, 2011). For adequate prevention, sound knowledge of the disease is very crucial. Knowledge of STI complication may play an important role in encouraging safer sexual behaviours (Mmbaga et al., 2007). Historically, knowledge about STI had been very low in communities where there is high prevalence of STI. Some communities viewed STI as unavoidable or as an "initiation into adulthood". In Tanzania, the prevalence of STI knowledge is very low (22.0%) (Mudassir et al., 2010; Mmbaga et al., 2007). Also in Nepal, the knowledge about STI is low (about 40%) (Jaiswal et al., 2005).

In Nigeria, 62% of young women and 40% of young men lack knowledge of STIs (National Population Commission, 2004). More importantly, report on STIs knowledge in southwest Nigeria is scanty and that of Ekiti land is not available. The purpose of this study was to assess the level of knowledge of STIs and possible factors associated with the knowledge of patients attending outpatient clinics in the University Teaching Hospital, Ado-Ekiti, Nigeria. This will enable advocacy to be targeted on at risk population, in order to control STIs and prevent its possible sequelae.

## MATERIALS AND METHODS

### Study site

University Teaching Hospital, Ado-Ekiti, was established in January, 2008. It is located in Ekiti State in the South-western part of Nigeria. It receives referral from Kogi, Osun, Ondo and Kwara States of Nigeria.

### Study design

The study was a cross-sectional descriptive study conducted from February to July, 2010. The study was carried out at the General Outpatient, Urology, Antenatal and Adolescent clinics of the hospital. Patients aged 10 years and above, that attended the above clinics (not necessarily for STIs), were enrolled for the study after obtaining voluntary written informed consent from each participant or their parent/guidance in patients less than 18 years. Those that did not give consent were excluded. In addition, ethical approval was also obtained from the Ethical and Research committee of the hospital. Participants were interviewed based on a pretested structured questionnaire with the assistance of trained and tested research assistants. In all, twenty-nine questions were administered (Appendix). Data were entered, checked and analysed using Statistical Package for Social Sciences for Windows 13.0 (2004). Frequency distributions of all categories of STI knowledge were computed. Chi square test was used to determine the strength of association of age group, educational level, occupational pattern, sources of information with STI knowledge.

## RESULTS

Out of the 592 interviewed, 242 (40%) were males while 350 (59.1%) were females. The total number of respondents with knowledge of STIs was 481 (81.2%) while 111 (18.8%) had no knowledge of STI. Figure 1 shows the age-specific prevalence of knowledge of STIs. The highest prevalence was in the age range 25 to 54years while the lowest was noted in the adolescents and youths (age group 10 to 24years). ($\chi^2$ = 14.343; P < 0.05). Figure 2 is a chart showing the knowledge of STIs according to educational level. Respondents in post-secondary level have the highest knowledge of STIs with a prevalence of 85.4%, while the lowest was with respondents with no education with prevalence of 72.7%; ($\chi^2$= 9.572, P > 0.05). Figure 4 is a chart showing the occupational pattern of knowledge of STIs. The drivers appeared to have the highest knowledge of STI with a prevalence of 90.9% while the lowest was the artisans with prevalence of 72.5%; ($\chi^2$ = 10.188, P < 0.05). Figure 5 shows a pie chart of the sources of information about STI. The highest source of information was through the news media followed by the hospital (P > 0.05).

## DISCUSSION

Although this is an hospital based study, the finding of high prevalence of knowledge of STIs in this environment is quite encouraging, especially when compared with that of Tanzania and the report on Nigeria (National Population Commission, 2003). However, it is worrisome to note that the knowledge of STIs was relatively low in the adolescents and the youths which are the future of any nation. This observation might mean that the adolescents and the youths in this environment are more prone to STIs with their attendant complications (P < 0.05) (Richard and Jay, 2002; Gerald and Steven, 2002; Whitfield, 1986; De Schryver and Meheus, 1990; Chamberlain, 1995; Westrom and Mardh, 1990; Rice, 1991; Robinson and Ridgeway, 1996; Otolorin, 1999). The low prevalence recorded in this study is similar to the

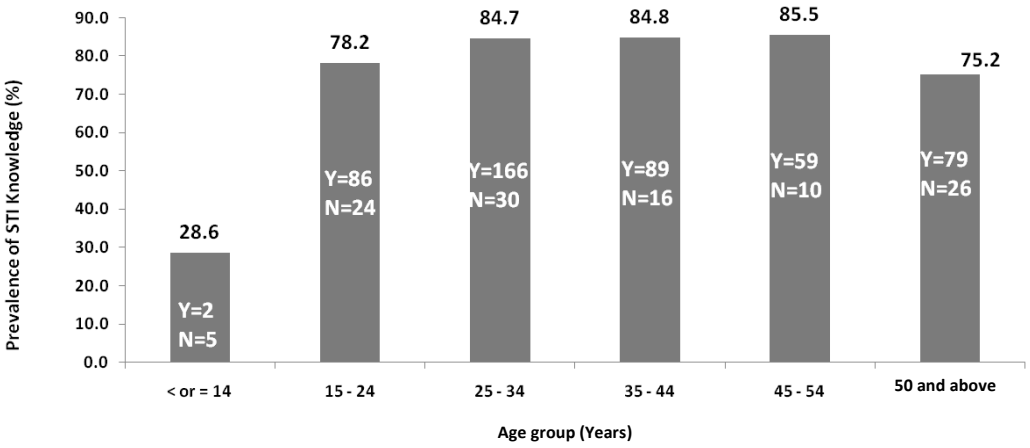


**Figure 1.** Age-specific prevalence of STI knowledge.

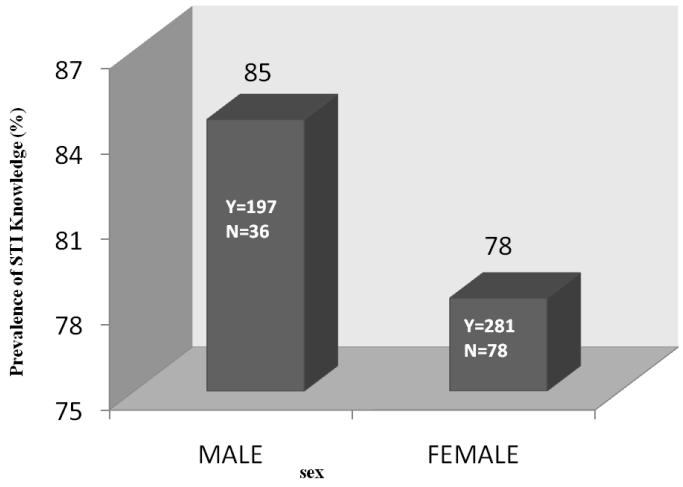


**Figure 2.** Prevalence of STI knowledge according to sex

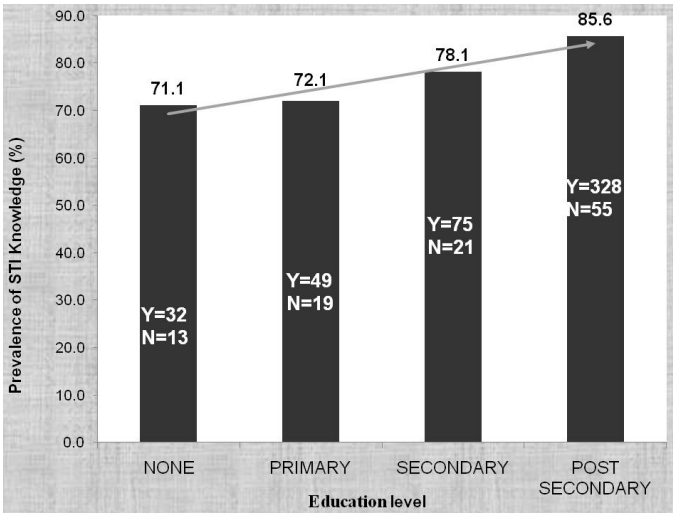


**Figure 3.** Prevalence of STI according to educational qualification.

findings in Malaysia which is a developing country like Nigeria (Mudassir et al., 2010). Therefore, awareness exercise must be targeted at the youths and the adolescents in this environment to control STIs.

This study has revealed that educational level is a key factor in acquiring knowledge of STIs because Figure 3 has shown that the higher the education, the higher the knowledge, even though not statistically significant; this is a similar trend observed in Ecuador (Nsuami et al., 2010; Solomon et al., 2007). The fact that our findings was not statistically significant ($p > 0.05$) may be due to the limited samples collected because the more educated one is, the more one is able to acquire knowledge, and poorer knowledge has been found to be associated with lower educational level (Solomon et al 2007).

Further more, the commonest source of information in this environment was found to be through the news media. This is not surprising because apart from the fact that many people possess small transistor radio all over the community, the advent of information and communication technology (ICT) has made information easier to acquire any where as a result of the in-built radio in the telephone handsets, which are commonly available in this community. This finding is in keeping with the result of the study conducted in southeast Nigeria (Obiechina et al., 2001). Since the next source of information is the hospital, health workers should find a way of giving information to their patient, especially on STIs, so as to improve the patient's knowledge. This may be done through regular health talks or distribution of literatures.

In addition, awareness may be created also by the health workers disseminating information to the rural populace through the churches, mosques or the markets. It is important for health workers to note that studies have shown that educating patients about STIs, which may be by mere explaining literature on it in a simple and direct manner, may foster a trusting patient/provider relationship throughout the health-seeking encounter (Johnson-

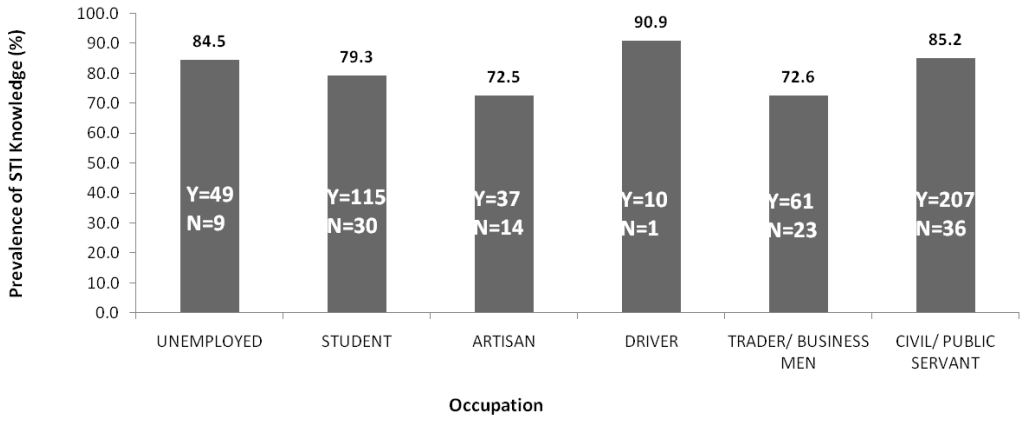


**Figure 4.** Prevalence of STI according to occupation.

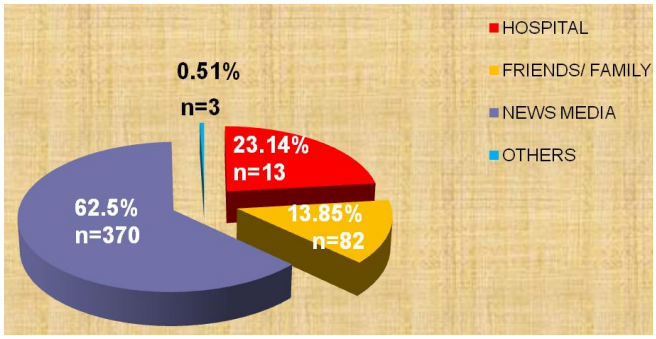


**Figure 5.** Sources of STI information.

Mallard et al., 2007). However, a study on how effective health education may be on the prevalence of STIs in this environment is highly desirable.

Finally, this study has shown that the drivers have more knowledge about STIs than any other occupation. This may not be unconnected with the easy access they have to car or handset radio, as many of them move within the state and outside the state wherefore they have opportunity to listen to news. A study to actually determine the reason for this high prevalence would be undertaken in a future study. It is therefore not out of place to target advocacy at various occupational group for effective control of STIs.

## Conclusion

The prevalence of knowledge of STIs is high (81.2%) among patients attending Outpatient clinics of University Teaching Hospital, Ado-Ekiti, Nigeria, especially among the age group 25 to 54. However, the prevalence among the adolescents who are the most vulnerable is relatively low. Age, educational level and sources of information are important factors affecting the knowledge of STIs.

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*Full Length Research Paper*

# Multiple outcome parameters: A 10 year follow-up study of first-episode schizophrenia

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**Schizophrenia is a disease with multiple dimensions, thus its treatment also results in differential outcomes. A number of clinically recovered patients do not recover in several other parameters of social functions which are necessary to lead a socially integrated and functional life, for example, the ability to work or live independently. Until recently, the outcome of schizophrenia has been measured primarily in terms of clinical symptoms. Although there have been revolutionary advances, it is undetermined, the extent to which these patients recover on both clinical and social parameters. This paper examines the status of comprehensive recovery on clinical and social parameters in hospitalized first-episode patients of schizophrenia in a long-term follow-up. 116 patients with first-episode schizophrenia in Mumbai, India, were followed for 10 years. Patients were assessed using clinical and psychopathological dimensions to determine levels of clinical and social recovery. Good outcomes on clinical parameter were seen in 61% of patients, while 46.7% obtained good quality of life, and 72.9% out of the total 116 patients were able to live independently; however, a significant number of these patients were still living with distressing residual symptoms, such as aggression, suicidality, and negative symptoms. The findings show that patient's exhibit differential outcome on multiple parameters, and a significant number continue to live with distressing symptoms, despite continued treatment for long periods. More research is required in outcome measures of response to treatment in schizophrenia, which can represent the real-life situation of these patients.**

**Key words:** Long-term outcome, clinical recovery, social recovery, multidimensional outcome, schizophrenia.

## INTRODUCTION

Schizophrenia is a severe mental disorder most commonly affecting young adults, typically in their twenties (Hegarty et al., 1994). Unfortunately, outcomes of schizophrenia continue to be unfavorable, as very few treatments are effective on all dimensions of the illness. Existing studies suggest that despite revolutionary advances, good clinical outcome (for example, improvement in symptoms) of schizophrenia remains limited (Harrow et al., 2005; Abdel-Baki et al., 2011), while far fewer patients improve in social functions (for example, employment, independent living). A number of patients do not fully improve even after receiving treatment, and many patients live with residual or persisting symptoms as a result (Emsley et al., 2011; Shrivastava et

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al., 2010; Andreason et al., 2005).

'Favorable' and 'unfavorable' outcomes depend upon the definitions of the outcome measures; therefore, it remains a matter of considerable debate on what outcome parameters of schizophrenia need to be measured (Ho et al., 2001; Karow et al., 2012; Hofer et al., 2011) which can reflect a real-life comprehensive outcome. A recent study from India showed that, half of the patients who 'recovered' were still exhibiting persistent residual symptoms, suggesting that patients may not recover equally in symptom remission and functionality despite responding to medication (Karow et al., 2012). As such, some patients may respond to all aspects of clinical, social and functional recovery; however, others may only recover in one of these aspects (Bromley and Brekke, 2010; Andreason et al., 2011; Meltzer, 1995).

Many patients shift from remission to relapse during the periods between follow ups. A study by Wunderink et al. (2009) examined the validity of remission in a large community. It was observed that patients fulfilling symptomatic remission criteria subsequently moved out of functional remission, nevertheless, those that did not fulfill functional remission criteria moved into the symptomatic remission category over a period of follow-ups. This demonstrates a significant overlap between remitted and unremitted subjects (Albert et al., 2011). It is therefore evident that remission is not a clinically stable state but rather much more variable than previously assumed.

Outcome research continues to be re-examined and re-defined, and recovery on social parameters is an important consideration (Emsley et al., 2011). The present study examines three indicators of social recovery: work ability (employment), independent living and family burden. Considering these social parameters, along with outcome on clinical parameters, these two measures represent comprehensive recovery. Employment is frequently stated as a goal of people diagnosed with schizophrenia (Schennach et al., 2012). There are wide variations in reported employment rates of schizophrenia patients among different countries. Most recently, European estimates of employment rates within the schizophrenic population range from 8 to 35%, while the rates in the United States are less clear (Marwaha and Johnson, 2004).

In a large community based study from China, (393 people with schizophrenia, 112 of which were never treated) it was reported that rural and urban residents had similar impairments due to symptoms, yet rural residents were three times more likely to be employed (adjusted relative risk 3.27, 95% CI: 2.11 to 5.07, $p < 0.001$) (Yang et al., 2012). Previous studies have shown that overall employment of persons with schizophrenia seems to be impeded by clinical problems, namely positive and negative symptomologies and poor neurocognitive functioning which have also been documented as predictive factors for employment status (Schennach et al., 2012).

Independent living has consistently been shown to be a marker of successful outcomes (Warner, 2009). In a 15 year follow-up study by Brown and Birtwistle (1998), it was found that only 19% of schizophrenia patients lived alone, suggesting poor independent living, while 55% were still living with families. Independent living involves dealing with complex personal and social issues and is one of the parameters representing high levels of self-care and the ability to undertake responsibility (Nadine and Medalia, 2004).

In addition to the ability to live independently, family burden is another parameter on which outcome has been measured (Perlick et al., 2006). Living with family, with the exception of living with a partner, is associated with an increased likelihood of recovery (Grandon et al., 2008). This may reflect better social support, which enables better social recovery. In spite of these benefits to the patients, caregivers often experience despair, anger, stress, and reduced quality of life. In a recent study, regarding burden and coping strategies of caregivers, findings revealed that 31.3% caregivers felt distress and 33.3% found stigma upsetting (Tan et al., 2012). Only 14.7% sought help from healthcare workers and 49.3% were interested to know more. Nevertheless, 24.7% verbalized sufficient social support.

As the burden of care giving intensifies, there is an increased propensity for the patient to experience relapse. Therefore, reducing family burden is an important prospective indicator of recovery, and also as an indicator of recovery itself, as it signals the ability and skills of the patient to live more independently with less reliance on family members.

The numbers of patients who recover clinically do not attain significant social and functional recovery, contrarily, socially recovered and functional patients also remain with residual symptoms, suggesting limited clinical recovery. If that is the case, fewer numbers of patients are likely to recover on comprehensive multidimensional parameter. We hypothesize that a far fewer number of patients will attain both social and clinical recovery. Further, fewer numbers of patients will recover when outcome is measured on multiple parameters. This paper examines the comprehensive recovery in a long-term, 10 year follow-up of hospitalized first episode schizophrenic patients.

## MATERIALS AND METHODS

This is a cross-sectional study of outcome measurement as per defined criteria on clinical and social parameters of patients who were available at the end of ten years follow up of a cohort of first episode schizophrenia. The study is a part of longitudinal long-term follow-ups study of schizophrenia. Base-line data of patients, who entered this study, was utilized for comparison between baseline and current assessment.

### Setting

This study was carried out in Silver-Mind Hospital which is a non-governmental hospital, certified as a psychiatric facility by the State Government, as per the Indian Mental Health Act, 1983. The study started in 1992 and was completed in 2005. The study was approved by the Independent Ethics Commission of Mumbai.

### Participants

Participants were hospitalized first-episode patients with schizophrenia. These patients were followed up for a period of ten years. Consenting patients were screened and recruited based on a confirmed diagnosis of schizophrenia as per Diagnostic and statistical manual of mental disorders- fourth edition (DSM-IV) (American Psychiatric Association, 2000), and demonstrated more than 80% compliance with treatment as per patients self-reports, and relatives' statements. These patients were primarily treated with antipsychotic medications, mostly the second generation antipsychotic drugs. They received social treatment in terms of individual family support. There was no structured case management or psychotherapies, except in the first two years of treatment. These patients were subsequently assessed on parameters of psychopathology and social functioning. The mean age of participants was 28.8 years (standard deviation (SD) = 8.2) and the mean illness duration was 12.7 months (SD = 7.3). Patient's characteristics are available in Table 2. The results revealed that 61 of the 101 patients showed 'improvement' on Clinical global impression scale (CGIS) at the end of ten years. During the course of the illness amongst the 101 patients, 36% of patients were never re-hospitalized after initial hospitalization.

### Clinical and social assessment parameters and outcome criteria

Clinical outcome was measured using CGIS (Guy, 1976). The clinical outcome measures or clinically good outcomes were indicated by a score of two or less on the CGIS, which meant they were showing "improvement" or "much improvement" on the CGIS between baseline and follow-up. Psychopathology was measured as follows: positive symptoms, negative symptoms and cognitive disorganization, which were assessed using the Positive and negative syndromes scale (PANSS) (Kay et al., 1987). Similarly, the general psychopathology (GP) subscale of PANSS was also used; depressive symptoms were assessed using the Hamilton depression rating scale (HDRS) (Hamilton, 1960); aggression, hospitalization, and suicidality were measured on a scale of 1 to 5 (1 being minimal functioning and 5 being high functioning), and global functioning was assessed by Quality of life (QOL) (WHO-BREF, 1993), as well as the Global assessment of functioning (GAF) (Guy, 1976).

We considered improved functioning as a score of less than 80 on the GAF and greater than 80 on the QOL scale at the end of the ten years. Of particular importance were the three psychopathological and social parameters namely, work ability, independent living and family burden (Table 3). Disturbed independent living (DIL), interpersonal/social functioning (IP), family burden and work ability were assessed using a scale of 1 to 5 (1 being minimal functioning and 5 being high functioning), this was locally tested in earlier studies (Shrivastava and Gopa, 2000).

### Statistical analysis

Descriptive statistics (paired *t*-tests) for characteristics of patient's scores were calculated at baseline and again after the ten year follow-up. Logistic regression and stepwise logistic models were used to evaluate invariable associations between baseline characteristics and recovery as defined by the CGIS (≤ 2).

## RESULTS

### Overall outcome

Clinically good outcomes, as determined by CGIS scores of two or less, were seen in 61% of patients. Significant improvement in GAF was seen over the 10 years, with 61.7% of patients having scores less than 80. Additionally, 46.7% of patients had achieved good QOL at the end of the 10 year follow-up (scores greater than 80). On the other hand, 39% of patients continued to experience symptoms of aggression, and 53.1% had incidences of suicidality. With respect to symptomologies, there were significant decreases in the total PANSS score (106.0 to 51.6, $p < 0.001$), positive symptoms scores (28.3 to 8.7, $p < 0.001$), negative symptoms score (23.5 to 12.2, $p < 0.001$), scores on the general psychopathology parameter of PANSS (54.3 to 29.1, $p < 0.001$), and scores on HDRS (17.5 to 13.1, $p < 0.001$). These can be seen in Table 1. GAF also showed significant improvement (48.3 to 78.9, $p < 0.001$). In addition to this, 48.5% were able to live independently, 40% were re-employed, and the number of patients who were a burden on family members had significantly decreased (96 to 46%, $p < 0.001$).

### Clinical outcome

In a comparison of patients who were classified as recovered based on CGIS scores versus non-recovered on CGIS scores at follow-up, those who recovered were more likely to have quality of life scores greater than or equal to 80, indicative of improved quality of life, compared to those who did not recover (Table 2). Additionally, those in the CGIS non-recovered group were much more likely to display symptoms of suicidality at the endpoint than those in the CGIS recovered group. There were no other significant differences between the two groups on clinical symptoms.

When looking at the number of clinical parameters on which patients were considered recovered, those classified as recovered on the CGIS did tend to have a higher number of recovered parameters; only 13.1% were not recovered on any parameters versus 27.5% of the CGIS non-recovered group; although this was not a significant difference. Both non-recovered and recovered CGIS patients exhibited equivalent recovery on at least 1 parameter (55 and 45.9%, respectively), yet recovered CGIS patients tended to have greater improvement when considering 2 (31.2% for recovered, 15% for non-recovered)

**Table 1.** Comparison of outcomes between baseline and follow-up.

| Outcome | Baseline | Follow-up | P value |
|---|---|---|---|
| | M (SD) | M (SD) | |
| PANSS | 106.0 (13.9) | 51.6 (8.9) | <0.001 |
| Positive symptoms | 28.3(5.1) | 8.7 (3.9) | <0.001 |
| Negative symptoms | 23.5 (6.9) | 12.2 (7.4) | <0.001 |
| GP | 54.3 (16.8) | 29.1 (11.9) | <0.001 |
| HDRS | 17.5 (6.1) | 13.1 (5.2) | <0.001 |
| GAF | 48.3 (11.0) | 78.9 (11.7) | <0.001 |
| | n | n | |
| Work ≤ 3 | 74 | 75 | 0.842 |
| DIL ≤ 3 | 89 | 48 | <0.001 |
| Aggression>2 | 64 | 39 | <0.001 |
| Family burden>3 | 4 | 54 | <0.001 |
| Suicidality>1 | 73 | 51 | <0.001 |

M = mean, SD = standard deviation. PANSS - Positive and negative syndrome scale; GP - General psychopathology subscale of PANSS; HDRS - Hamilton depression rating scale; GAF - Global assessment of functioning; IP Social - Interpersonal/Social; DIL = Disturbed independent living.

**Table 2.** Comparison of clinical parameters between recovered and non-recovered patients.

| 10 year outcome | Clinical recovery (CGIS) (%) | | |
|---|---|---|---|
| | Not recovered (n=40) | Recovered (n=61) | P Value |
| GAF≥80 | 22 (61.1) | 37 (61.7) | 0.957 |
| QOL≥80 | 0 (0.0) | 28 (46.7) | <0.001 |
| Positive symptoms>21 | 0 (0.0) | 0 (0.0) | - |
| Negative symptoms>21 | 5 (12.5) | 7 (11.5) | >0.999 (Fisher's exact) |
| HDRS>17 | 10 (25.0) | 12 (21.1) | 0.648 |
| Suicidality>1 | 36 (90.0) | 15 (24.6) | <0.001 |
| | Clinical parameters showing recovery (%) | | |
| None | 11 (27.5) | 8 (13.1) | 0.111 |
| 1 | 22 (55.0) | 28 (45.9) | 0.564 |
| 2 | 6 (15.0) | 19 (31.2) | 0.103 |
| 3 | 1 (2.5) | 6 (9.8) | 0.165 |
| 4 | 0 (0.0) | 0 (0.0) | |

recovered) or three (9.8% for recovered, 2.5% for non-recovered) parameters, but again these differences were not significant. Neither groups demonstrated recovery on four or more parameters (Table 2).

## Social outcomes

In terms of work ability and employment, there was a significant difference in skills necessary for employment in those patients who had recovered (40%), compared to those who were not recovered (25%). In a comparison of patients who were classified as recovered based on CGIS scores versus non-recovered on CGIS scores, those who recovered were more likely to have an independent living score higher than 3 (72.9%) compared to those who were not recovered (12.5%) (Table 3). The CGIS recovered and CGIS non-recovered groups did not differ significantly on family burden scores (46.7% for recovered versus 38.9% for non-recovered).

When looking at the number of social parameters on which patients were considered recovered, almost half (45.0%) of the CGIS non-recovered group did not show recovery on any of the social parameters, which differed

**Table 3.** Comparison on social parameters between recovered and non-recovered patients.

| 10 year outcome | Not recovered (%) (n=40) | Recovered (%) (n=61) | P value |
|---|---|---|---|
| Independent>3 | 5 (12.5) | 43 (72.9) | <.001 |
| Work>3 | 1 (2.5) | 24 (40.0) | <0.001 |
| Family burden≤3 | 14 (38.9) | 28 (46.7) | 0.457 |
| **Number of social parameters showing recovery (%)** | | | |
| None | 18 (45.0) | 3 (4.9) | <0.001 |
| 1 | 20 (50.0) | 26 (42.6) | 0.630 |
| 2 | 2 (5.0) | 26 (42.6) | <0.001 |
| 3 | 0 (0.0) | 6 (9.8) | 0.046 |

significantly from 4.9% of the CGIS recovered group ($p < 0.001$) (Table 3). There was no significant difference between both CGIS recovered and CGIS non-recovered groups on one outcome parameter (42.6 and 50%, respectively, $p = 0.630$). While 42.6% of CGIS recovered patients showed recovery on two parameters, 5% of CGIS non-recovered patients recovered on two parameters ($p < 0.001$). Additionally, 10% of CGIS recovered patients had improvement on all three social parameters classifying them as fully recovered, while none of the CGIS non-recovered group showed recovery level scores on all three social parameters ($p = 0.046$) (Table 3).

### Multidimensional outcome

As anticipated, recovery was associated with an increasing number of these three parameters showing recovery ($p < 0.001$). Of the 101 subjects, there were 18 (17.8%) who did not recover clinically and did function satisfactorily in these three social parameters (see non-recovered column of Table 3). On the other hand, there were 32 (52.4%) of the subjects who recovered clinically and functioned satisfactorily on two or three of these social parameters. Only two of the clinically non-recovered patients functioned satisfactorily on two social criteria.

## DISCUSSION

We found that 61% of patients showed improvement over the course of the ten years with respect to clinical parameters. Of particular importance was that participants improved greatly in suicidality and QOL, yet the majority of participants tended to recover on only one clinical parameter, and none recovered on more than three parameters. Many long-term outcome studies from India have reported similar favorable outcomes results, ranging from 22 to 75% (Susser et al., 1998; Varma et al., 1997). The Madras longitudinal study (Thara, 2004) from India reported good outcomes as high as 75%, which were accompanied by significant numbers of patients finding employment 10 to 15 years later. This rate of remission is parallel to rates reported from urban and rural Chandigarh as part of the Determinants of outcome of severe mental disorders (DOSMeD) project (Craig et al., 1997); nonetheless, these numbers are lower than the 69% remission rate recorded in Vellore, in the Study of Factors affecting the course and outcome of schizophrenia (SOFACOS) in the early 1980s (Verghese et al., 1989). This is consistent with the favorable outcome hypothesis in low and middle-income countries found in previous literature (Kulhara, 1994; Malhotra et al., 1998; Varma et al., 1996; Susser et al., 1995).

A significant proportion of first-episode schizophrenia pa-tients achieve a moderate to long-term outcome, which results in stability of global functioning rather than dete-rioration, as shown in most industrialized countries (Wallace et al., 2000). There is a growing interest in identifying and surmounting barriers to employment for people with schizophrenia. Our finding of good outcomes in 61% of patients after ten years is consistent with what has been previously reported.

In the present study, among those who recovered on the CGIS, we found that 72.9% were living independently. Independent living has consistently been shown to be a marker of successful outcomes, as it involves abilities of self-care, undertaking responsibilities, and dealing with complex personal and social issues (Wallace et al., 2000). In a 15 year follow-up study by Brown and Birtwistle (1998), it was found that only 19% of patients lived alone, suggesting poor independent living, while 55% were still living with families. Thus, our results show much higher levels on independent living than seen in previous studies. Perhaps the inclusion criteria of good compliance with treatment in the present study led to this finding, or there may be other cultural or contextual factors that predispose some groups of patients to higher rates of independent living.

In contrast to previous findings by Srinivasan and Thara (1997) who demonstrated robust employment rates from India in which they report an increase in employment rate to 53% in a long-term study, there were no improvements in work or employability skills in our total sample. However, when considering those who were clinically recovered, there were significant differences in employment, with 40% of recovered patients employed.

### Multidimensional outcome

We sought out to examine the number of patients who recovered on each of these three criteria alone (work ability, independent living and family burden), as well as on possible combinations of these three parameters. We found that when we combined clinical criteria with two or three other areas of social criteria, the recovery rate dropped to about 10 to 43% (see recovered column in Table 3). This study showed that approximately two thirds of patients recover on clinical aspects only, and by about one third on both parameters. In this study, 46% of patients showed a score of less than 80 on QOL in the recovered group. We then looked at how many patients showed improvement in symptoms, QOL, and level of functioning combined in the recovered group. We found that 45% of patients recovered on two parameters, and 31% recovered on three parameters (QOL and GAF) when taken together. Thus, a comprehensive social recovery occurred in a range of 31 to 45% of patients (Table 2).

Sartorius et al. (1996) found similar results of poor outcomes in chronic schizophrenic patients when followed up for an average of six years. They reported that depending upon the criteria applied, symptomatic remission at follow-up was observed in only 37 to 59% of the cohort. In addition to this, social-vocational recovery was observed in 31% of the cohort. Approximately a quarter of the patients achieved both symptomatic remission and social-vocational recovery; 78% of patients had a relapse during the period of follow-up, with only 3% rated as having a good outcome on the Global assessment scale (GAS).

Liberman and Kopelowicz (2005) compared remitted and unremitted patients and reported that a significantly better level of functioning was measured for remitted versus non-remitted patients, though these remitted patients still showed areas with an inadequate level of functioning. Functional deficits were most often seen in social relations (40%), work (29%) and daily life activities (17%). These findings are in line with the present study being that, at the end of ten years of reasonably continuous treatment, 40% of the patients still exhibited depressive symptoms, 24% presented with negative symptoms and 51% showed symptoms suggestive of suicide behavior, intent or occasional crisis. Moreover, amongst the subjects who showed clinical recovery, 21.1% showed depressive symptoms, 11.5% showed negative features and 24% showed symptoms of suicidality.

## Conclusion

This study has shown that when clinical and social parameters of outcome are combined, outcome rates drop significantly. Though there is significant overlap between these aspects, all subjects achieving symptomatic remission do not necessarily gain social recovery as well. A significant number of patients, despite recovery, still live with persisting symptoms of aggression, depression and a range of suicidal tendencies. Since patients achieve different level of outcome on different parameters, clinical recovery only cannot be sufficient enough to represent a correct state of outcome. It is therefore important that outcome should be measured on multiple parameters, most importantly of clinical and social parameters. Further research is required in this area to decide on what parameters of outcome of schizophrenia should be measured.

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*Full Length Research Paper*

# A Bayesian Poisson specification with a conditionally autoregressive prior and a residual Moran's coefficient minimization criterion for quantitating leptokurtic distributions in regression-based multi-drug resistant tuberculosis treatment protocols

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**In this study, we employed an eigenfunction decomposition algorithm associated with a Moran's coefficient to investigate district-level non-linearity in an empirical dataset of spatiotemporal-sampled MDR-TB parameter estimators sampled in San Juan de Lurigancho (SJL) Lima, Peru. The non-parametric technique attempted to remove the inherent autocorrelation in the model by introducing appropriate synthetic surrogate variants. We also constructed a robust Bayesian Poisson model to generate unbiased estimators for qualitatively assessing resistance to four commonly used drugs in TB treatment: isoniazid, rifampin, ethambutol, and streptomycin. Initially, data of residential addresses of individual patients with smear-positive MDR-TB were geocoded in ArcGIS. Next, the sampled data were matched automatically and interactively within the geodatabase. The MDR-TB data feature attributes were then calculated and digitally overlaid onto sub-meter resolution satellite data within a 1 km buffer of 31 georeferenced health centers using a 10 $m^2$ grid-based algorithm. Global autocorrelation statistics were then generated by decomposing the sampled data into positive and negative spatial filter eigenvectors using the eigenfunction decomposition algorithm. Bayesian Poisson projections were then rendered employing normal priors for each of the sampled estimators. A Residual Moran's coefficient (MC) minimization criterion was then applied to the clinical coefficients generated from the decomposition algorithm to detect any unaccounted latent autocorrelation error in the estimators. The model accounted for approximately 14% pseudo-replicated information and exhibited positive residual autocorrelation. Spatial statistics can elucidate the mechanics of MDR-TB transmission by prioritizing clinical covariates for identifying spatial distribution of high- risk populations and random heterogeneity in resistant strains.**

**Key words:** Multi-drug resistant tuberculosis, Bayesian Poisson, residual Moran's coefficient (MC), minimization criterion, San Juan de Lurigancho (SJL) Lima, Peru.

## INTRODUCTION

Multiple linear regression analysis techniques coupled with normal probability models have become standard epidemiological tools to quantitatively analyze spatiotemporal-sampled clinical and environmental covariates associated with multi-drug resistant tuberculosis (MDR-TB) for identifying high-risk populations (Smith, 1994; Johnson, 2003;

Clarke et al., 2002; Akashi et al., 1996; Barr et al., 2000). MDR-TB is defined as TB that is resistant to isoniazid (INH) and rifampicin, which most commonly develops in the course of TB treatment (Iseman, 1993). Generalized linear models (GLMs) represent a class of fixed effects regression models for several types of dependent variables (e.g., continuous, dichotomous, counts). For example, El Sahly et al., (2006) analyzed molecular epidemiological techniques of MDR-TB employing a case–control study of 2,170 patients with drug- susceptible TB in Houston and Harris County, Texas, from 1995 to 2001 using a multivariate logistic regression where drug resistance was the categorical dependent variable. Cases with various forms of resistant TB were also compared to a control group which consisted of patients with culture positive, drug susceptible TB, with respect to sociodemographic, clinical and strain-stratified genotype-dependent explanatory predictor variables using bivariate chi-square and univariate statistics. As part of the study, patients were identified as drug-resistant cases if they had a positive culture for an MDR-TB strain that was resistant to any of the following: isoniazid, rifampin, ethambutol or streptomycin. In the analyses, the variables that showed a colinearity coefficient of 0.3 or more were eliminated. Thereafter, the multivariate logistic model constructed employing the explanatory predictor variables associated with drug resistance revealed a *P* value of ≤0.1. In the final model, *P* values of ≤0.05 were considered significant. The regressed residual MDR-TB covariates revealed that the observational predictors related to human immunodeficiency virus (HIV) seropositivity, Hispanic ethnicity, Asian ethnicity and a history of past TB were associated with some parameter estimators, whereas, being foreign born having a history of past TB, and younger age were definitive estimators (i.e., P< 0.050). The model revealed that the ethnic groups may have been more affected by TB because of the propensity of HIV among these sampled populations. Moreover, the authors identified that patients with AIDS and other disseminated immunodeficiency disorders were at an increased risk of acquiring drug resistance particularly rifampin while on therapy.

Although linear mixed models are widely used in MDR-TB which can handle non-normal data by using link functions and exponential family (e.g. normal, Poisson or binomial distributions), the assumptions underpinning multiple regression necessarily impose several important constraints that may not always be satisfied or, that might at least require careful consideration when modeling time-series dependent MDR-TB clinical and /or environmental covariates. For example, commonly, the relationships between the outcome and the explanatory predictor variables in a robust spatiotemporal MDR-TB model constructed from multiple regression-based residuals are assumed to be linear and the residual error variance estimates are assumed to be the same, regardless of the value of the sampled clinical and /or environmental covariate coefficients. Also, commonly in a linear, time-series dependent MDR-TB predictive regression equation, the error residuals in the model are assumed to be normally distributed and the sampled estimators are assumed to be independent. However, this may not always be the case in spatiotemporal MDR-TB regression-based modeling since many sampled clinical and/or environmental covariate coefficients may exhibit non-linear feature attributes. As such, although the estimated regression coefficients may be unbiased in the MDR-TB model they will not express the minimum variance among all estimates. Further, the mean squared error would also tend to underestimate the variance in the model. This would lead directly to overestimation of the sampled parameter estimator significance levels which, in turn, would result in underestimation of confidence intervals thus, leading to underestimation of the test statistics for the F test. The F-test is sensitive as it is commonly quantitated by considering a decomposition of the variability in a collection of data in terms of estimable functions and their associated sum of squares (Dorman 2007).

Estimable functions are functions of model parameters (e.g. difference between two parameters, difference between a parameter and the difference of two others, etc.) that are invariant regardless of the generalized inverse employed. The GLM, VARCOMP, and other SAS/STAT procedures label the Sums of Squares associated with the various effects in the model as Type I, Type II, Type III, and Type IV (www.sas.edu). For example, in the Type I form of sum of squares (i.e., the hierarchical decomposition of the sum-of-squares method), each sampled MDR-TB term would be adjusted for only the term that precedes it in the model. Type I sums of squares could then be used for constructing a balanced ANOVA time series-dependent MDR-TB model in which the main effects in the sampled data would be specified before any first-order interaction effects are quantitated. Thereafter, any first-order interaction effects in the model would be specified before any second-order interaction effects, and the second-order interaction effects would be specified in the model before the third-order interaction effects, and so on. A polynomial time-series dependent MDR-TB regression model for any lower-order terms could also be specified before any higher-order terms are quantitated. Further, a purely nested MDR-TB model in which the first-specified effect is nested within the second-specified effect may also be determined. For defining a Type II sums of squares in a spatiotemporal MDR-TB model a method can be employed which calculates an effect that can be adjusted for by all other "appropriate" effects in the model. An appropriate effect is one that corresponds to all effects that do not contain the

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effect being examined (Cressie 1993). The Type II sum-of-squares method could then be used for deriving robust unbiased estimators in a balanced ANOVA time series dependent MDR-TB model and/or any MDR-TB model with purely nested design.

Type III estimable functions for sum of squares (i.e., the default method) can also be utilized for regressing time series dependent MDR-TB for modeling clinical and environmental exploratory covariates. This method can calculate the sums of squares in a time series dependent MDR-TB model using an effect in the design matrix of the model. The Type III sums of squares have one major advantage for spatiotemporal MDR-TB modeling in that they are invariant with respect to the cell frequencies as long as the general form of estimability remains constant. Hence, this type of sums of squares would be considered useful for an unbalanced spatiotemporal MDR-TB model with no missing cells. In a factorial design with no missing cells, this method would be equivalent to the Yates' weighted-squares-of-means technique. Today, by default, most major statistical programs perform unbalanced ANOVA based on Type III sums of squares (that is, Yates's weighted squares of means) (McPherson and Jetz 2007, Cressie 1993). The Type III sum-of-squares method could be used for any MDR-TB models listed in the aforementioned Type I and Type II specifications.

Finally, a Type IV estimable function can be designed for a situation in which there is a spatiotemporal MDR-TB model with missing cells. For example, for any effect *F* in an MDR-TB model design, if *F* is not contained in any other effect, then Type IV = Type III = Type II. When *F* is contained in other sampled MDR-TB effects, Type IV will distribute the contrasts being made among the sampled clinical and environmental parameter estimators in *F* to all higher-level effects equitably. The Type IV sum-of-squares method is commonly used for any models listed for Type I and Type II estimable functions. Fortunately, PROC GLM in SAS and the SAS regfunction in R both can calculate various F tests.

The F-test is designed to test if two population variances are equal (Homer and Lemeshew, 2000). The test does this by comparing the ratio of two variances. So, if the variances are equal in a spatiotemporal MDR-TB model, the ratio of the variances will be 1. Commonly, the F-test in one-way analysis of variance is used to assess whether the expected values of a sampled quantitative variable within several pre-defined groups differ from each other. For example, suppose that a medical trial compares four MDR-TB related treatments. The ANOVA F-test can be used to assess whether any of the treatments is on average superior, or inferior, to the others versus the null hypothesis that all four treatments yield the same mean response. This is an example of an "omnibus" test, meaning that a single test is performed to detect any of several possible differences.

Hypotheses regarding MDR-TB regression- based equality vs. inequality tests and between k expectancies $\mu_1=\mu_2=\ldots=\mu_k$ vs. $\mu_1\neq\mu_2\neq\ldots\neq\mu_k$ in ANOVA; or regarding equality between k standard deviations $\sigma 1=\sigma_2=\ldots.=\sigma_k$ vs. $\sigma_1\neq\sigma_2\neq\ldots\neq\sigma_k$ for testing equality of variances in ANOVA; or regarding the clinical and/or environmental covariate coefficients $\beta 1=\beta_2=\ldots.=\beta_k$ vs. $\beta_1\neq\beta_2\neq\ldots\neq\beta_k$ in multiple linear regression can be tested using omnibus" test (Fotheringham, 2002). Alternatively, pairwise tests could be carried out among the treatments (e.g., the MDR-TB trial example with four treatments is carried out using six tests pairs of treatments). The advantage of the ANOVA F-test for spatiotemporal MDR-TB modeling is that there is no requirement to pre-specify which treatments are to be compared, and there is no need to adjust for making multiple comparisons. The disadvantage of the ANOVA-MDR-TB related F-test is that if the null hypothesis is rejected in the time series data, the residuals would not be able to determine which treatments are significantly different from the others. If the F-test is performed at level α we cannot state that the treatment pair with the greatest mean difference is significantly different at level α (Hosmer and Lemeshew 2000). Thus, although the F-test can be used to compare nested models, in an asymptotic or approximate fashion to test the hypothesis that the simpler of the time series dependent MDR-TB models is sufficient to explain the data, for example, the residuals may have correlated error. A variance decomposition may even be performed for generating inferences for the variances in the model but, sources of variation in multilevel regression MDR-TB can still occur.

Although the F statistics may not be exact, MDR-TB researchers to date have found that the F-ratios are acceptable unless the design is highly unbalanced. The F-ratio is used to determine whether the variances in two independent samples are equal (Cressie 1993). Ideally, this ratio should be approximately 1 in a spatiotemporal MDR-TB model if the corresponding effects are zero; otherwise the expected F-ratio will exceed 1. We would expect the F-ratio to be less than 1 only in unusual models with negative within-group correlations (e.g., if the spatiotemporal-sampled MDR-TB data have been renormalized in some way, and this had not been accounted for in the data analysis). When the null hypothesis of no group differences is true, then the expected value of the numerator and denominator of the F ratio will be equal (Hosmer and Lemeshew 2000). As a consequence, the expected value of the F ratio in a spatiotemporal MDR-TB model when the null hypothesis is true is also close to one. When the null hypothesis is false in the model and there are group differences between the means, the expected value of the numerator will be larger than the denominator. As such, the expected value of the F ratio will be larger and the MDR-TB model estimates will also more likely be larger than one under the null hypothesis. However, the point is that both the numerator and denominator in the MDR-TB model would be random variables and so would be the F

ratio. If we assume the null hypothesis is true in the time series dependent MDR-TB model one distribution will be determined, and if we assume that it is false with various assumptions about effect size, sample size, and so forth another distribution would be rendered. The F ratio is drawn from a distribution (Cressie 1993). Thereafter, an F value for the MDR-TB model can be determined. Fortunately, when the null hypothesis is false in the model it would be still be possible to get an F ratio less than one.

However, an F-ratio based on a mean square error (MSE) in a spatiotemporal MDR-TB model will not be able to disentangle the contribution of the experimental effect (i.e. the linear component) and the degree to which the treatment effect varies across participants/covariates (i.e. the non-linear participant by experimental-effect interaction). In an analogy to standard deviation, taking the square root of MSE in a spatiotemporal MDR-TB model will yield the root mean square error or root mean square deviation (RMSE), which has the same units as the quantity being regressed for an unbiased estimator. The RMSE is the square root of the variance, known as the standard deviation. Thus, a statistically significant effect in a spatiotemporal predictive regression-based MDR-TB model could be due to one of three things: (a) a significant experimental effect, (b) significant variation in the treatment effect across participants, or (c) both of these things. Unfortunately, the F ratio would not be able to differentiate the optimal residual forecasts from such distributions.

Further, if any of these tests are performed to determine the underlying assumption of homoscedasticity (i.e., homogeneity of variance), in the spatiotemporal MDR-TB model as a preliminary step to testing for mean effects, the residuals would reveal an increase in experiment-wise Type I error rate. Therefore, significance testing for quantitating resulting confidence regions and tests of the hypotheses employing combinations of sampled MDR-TB explanatory clinical and /or environmental covariate coefficients would be critically jeopardized. Violations of linearity are extremely serious in time series dependent infectious disease models as fitting linear data attributes to non-linear algorithms would render forecasts that are erroneous especially when extrapolation occurs beyond the range of the sampled data. For example, spatio-temporal MDR-TB statistics will not follow the F-distribution, under the null hypothesis in a time series dependent model unless the sums of squares are independent, and each follow a scaled chi-squared distribution. The latter condition, however, is only guaranteed if the sampled clinical data values are independent and normally distributed with a common variance.

Another common problem in the use of linear coefficients when modeling spatiotemporal-sampled MDR-TB data is the occurrence of covariates that are not independent (i.e., non-zero correlations amongst covariates) giving rise to multicollinearity. Multicollinearity increases the standard errors of the coefficients (Hosmer and Lemeshew 2000). Increased standard errors in turn means that the spatiotemporal-sampled clinical and environmental covariate coefficients for some independent variables may be found not to be significantly different from 0. Without multicollinearity and with lower standard errors, however these same coefficients and their null findings might have been found to be significant. In other words, multicollinearity in a spatiotemporal MDR-TB model would misleadingly inflate the standard errors.

Unfortunately, since the factors associated with the emergence of MDR-TB and their effects on the epidemiology of TB are complex and multi-faceted (e.g., poor medical management, lack of direct observed treatment, limited or interrupted drug supplies, poor drug quality, widespread availability of anti- TB drugs without prescription, dissociation between public and private sector, and poorly managed national control programmes (Espinal, 2001; Farmer et al., 2001), multiple parameter estimators are commonly employed in the regression uncertainty matrix often rendering serial correlation in the residual outcome explanatory predictor covariate dataset. When more than two covariates in a model are highly correlated, multicollinearity can occur (Miles and Shelving, 2001; Pedhazur, 1997; Slinker and Glantz, 1985).Collinearity and multicollinearity can seriously distort the interpretation of a spatiotemporal linear-dependent regression model (Cohen et al., 2003; Maddala, 2001; Chatterjee and Hadi, 1988). Traditionally, the role of each sampled covariate in a spatiotemporal time-series dependent MDR-TB regression model would be to increase precision, as expressed through a reduction in residual predictive error variance covariance matrix estimates, as well as, reduced bias in the sampled coefficients. Multicollinear MDR-TB clinical and environmental-related covariate coefficients however, would be difficult to analyze as their effects on a response variable could be due to either true synergistic relationships among the sampled covariates or, confounding effects creating spurious correlations.

In some sense, the collinear MDR-TB variables would contain the same information about the dependent variable in the spatiotemporal model. If nominally "different" measures actually quantify the same phenomenon then they are redundant (Glantz and Slinker, 2001; Fotheringham et al., 2002). Alternatively, if the time series-dependent MDR-TB explanatory predictor variables are accorded different names and perhaps employ different numeric measurement scales but, continue to maintain a high correlation with each other, the residuals would still suffer from redundancy. A principal danger of spatiotemporal data redundancy is overfitting in regression model frameworks. In statistics, overfitting occurs when a statistical model describes random error or noise instead of the underlying relationship (Dormann 2007; Homer and Lemeshew 2000; Cressie 1993; Manton and Stallard 1981). Additionally, when a spatiotemporal MDR-TB distribution model is excessively complex, such as a model with extensive parameter estimators relative to

the number of observations, biased predicted residual space-time autoregressive error estimates may be rendered by the model. Unfortunately this occurs commonly by exaggerating minor fluctuations inconspicuously in the sampled clinical and environment sampled data.

As such, separable approximations of non-separable space-time MDR-TB error covariance matrix estimates cannot be quantitated. Further, the nearest Kronecker product approximation in the time series cannot be determined especially in a MDR-TB dataset employing a Frobenius norm of a space-time error covariance matrix. The Kronker product is a generalization from vectors to matrices which renders the matrix of the tensor product (Fotheringham 2002). The Frobenius norm is the square root of the sum of the absolute squares of its elements (Cressie 1993). The tensor product, denoted by $\otimes$, may be applied in different contexts to vectors, matrices, tensors, vector spaces, algebras, topological vector spaces, and modules, among many other structures or objects (Griffith and Layne 1999, Cressie 1993 ). As such, in a hypothetical generalized MDR-TB bilinear operations model a function combining elements of two vector spaces (e.g., matrix multiplication) will not yield an element of a third vector space that is linear in each of its arguments. Thus, solutions preserving properties of residual space-time MDR-TB uncertainty covariance matrices, such as symmetry, positive definiteness, and other structures cannot be quantitated.

In linear algebra, a symmetric $n \times n$ real matrix $M$ is said to be positive definite if $z^{\mathrm{T}}Mz$ is positive, for any non-zero column vector $z$ of $n$ real numbers; where $z^{\mathrm{T}}$ denotes the transpose of $z$. More generally, an $n \times n$ complex spatiotemporal MDR-TB matrix $M$ would be positive definite if $z^*Mz$ is real and positive for all non-zero complex vectors $z$; where $z^*$ denotes the conjugate transpose of $z$. This property implies that $M$ is an Hermitian matrix. The conjugate transpose, or adjoint matrix of an $m$-by-$n$ matrix with complex entries is the $n$-by-$m$ matrix $A^*$ obtained from A by taking the transpose and then taking the complex conjugate of each entry (i.e., negating their imaginary parts but not their real parts) (Cressie 1993). The conjugate transpose would then be formally defined by where the subscripts in the MDR-TB model denotes the $i,j$-th entry, for $1 \le i \le n$ and $1 \le j \le m$, and where the overbar denotes a scalar complex conjugate. The complex conjugate of $a + bi$, where $a$ and $b$ are reals, is $a - bi$. (Cressie, 1993). This definition can also be written as $\mathbf{A}^* = (\overline{\mathbf{A}})^{\mathrm{T}} = \mathbf{A}^{\mathrm{T}}$ in a spatiotemporalMDR-TB modelwhere $\mathbf{A}^{\mathrm{T}}$denotes the transpose and $\overline{\mathbf{A}}$denotes the matrix with complex conjugated entries. Thus , a Hermitian MDR-TB matrix (i.e., self-adjoint matrix) is a square matrix with complex clinical and environmental covariate entries that is equal to its own conjugate transpose – that is, the element in the $i$-th row and $j$-th column is equal to the complex conjugate of the element in the $j$-th row and $i$-th column, for all indices $i$ and $j$: $a_{ij} = \overline{a_{ji}}$ .If the conjugate transpose of a matrix $A$is denoted by $A^\dagger$, then the Hermitian property can be written in a MDR-TB model concisely as $A = A^\dagger$ . for efficient predictive residual uncertainty quantification. Unquantitated hidden latent correlation error coefficients in spatiotemporal datasets of time series dependent covariate coefficients cangenerate misspecified estimates (Griffith, 2008).

Additionally, since one of the features of multicollinearity is that the standard errors of the affected regression residual coefficients tend to be large (Glantz and Slinker, 2001; Glantz and Amrhein, 1997), the test of the hypothesis that the sampled explanatory covariate coefficients would be equal to zero in a spatiotemporal clinical/environmental–oriented MDR-TB regression-based equation would then subsequently lead to a failure to reject the null hypothesis. In such circumstances, if the linear-dependent observational explanatory predictors are estimated, a covariate would still be found to be significant; specifically, a TB analyst will reject the hypothesis that the coefficient is zero. In statistics, simple linear regression is the least squares estimator of a linear regression model with a single predictor variable (Dutilleul 1993; Hosmer and Lemeshew, 2000). A simple linear regression fits a straight line only through the set of $n$ points in such a way that makes the sum of squared residuals of a model robust that is, vertical distances between the points of the spatiotemporal-sampled dataset and the fitted line are as small as possible (Fotheringham, 2002). As such, in the presence of multicollinearity, a TB analyst might falsely conclude that there is no linear relationship between an independent and a dependent variable in a spatiotemporal MDR-TB regression-based predictive risk-based model.

So long as the underlying specification is correct, however, multicollinearity will not actually bias spatiotemporal MDR-TB regression model residuals; it will just produce large standard errors in the related inde-pendent variables. If, however, there are other problems such as omitted variables which introduce bias in the model, multicollinearity can multiply the effects of that bias in the residuals by orders of magnitude within spatially autoregressive uncertainty dependent frameworks. Importantly, the common use of regression in spatiotemporal MDR-TB modeling exercises is to take sampled explanatory covariate coefficients rendered from the model residuals and then apply them to other non-linear higher order autoregressive matrices (e.g., block kriging). Kriging is a group of geostatistical techniques commonly employed to interpolate the value of a random field (e.g., the elevation, $z$, of the landscape as a function of a geographic sampled MDR-TB-related point) at an unobserved location from observations of its value at nearby locations (Fotheringham 2002). Thus, if the new MDR-TB data generated from a stochastic interpolation based algorithm, for example, differs in any way from the

linear dependent data that was initially fitted, large residual error coefficients will be introduced in the forecasts as the pattern of multicollinearity between the independent variables would be very different in the simulated MDR-TB data. Consequently, linear coefficients, based on collinear and multicollinear variables, can bias time series dependent MDR-TB explanatory clinical and/or environmental covariate coefficients yielding unstable, non-normal parameter estimators and unreliable autoregressive significance tests.

Further, the data regularization framework in such an interpolator may not recover well-behaved functional representations of the time series-dependent input MDR-TB data. Although the procedure would split the interpolation operator into a discrete deconvolution followed by a discrete convolution, misspecifications will still arise in the stochastic matrix within the probabilistic weighting scheme. As such, connections to radial basis functions will also be erroneous. Since the radial basis function is a real-valued function whose value depends only on the distance from the origin, so that $\phi(\mathbf{x}) = \phi(\|\mathbf{x}\|)$; or alternatively on the distance from some other sampled point *c*, so that $\phi(\mathbf{x}, \mathbf{c}) = \phi(\|\mathbf{x} - \mathbf{c}\|)$ (Cressie 1993), any function $\phi$ that satisfies the property $\phi(\mathbf{x}) = \phi(\|\mathbf{x}\|)$ in a spatiotemporal regression-based MDR-TB model is a radial function. Therefore, it would be difficult to posit a general framework for linking spatiotemporal MDR-TB statistical data analysis with approximation methods that are built on non-negative operators.

In mathematics, on a finite-dimensional inner product space, a self-adjoint operator is an operator that is its own adjoint, or, equivalently, one whose matrix is Hermitian(Cressie 1993). By the finite-dimensional spectral theorem, such operators can be only associated in a spatiotemporal MDR-TB model when employing an orthonormal basis of the underlying space in which the operator is represented as a diagonal matrix constructed from the covariate entries. In linear algebra and functional analysis, the spectral theorem is any of a number of results about linear operators or about matrices (Hazewinkle 2001). In broad terms the spectral theorem provides conditions under which an, operator or, a time series dependent MDR-TB matrix can be diagonalized. This concept of diagonalization would be relatively straightforward for operators on finite-dimensional spaces, however this would require some modification for operators on infinite-dimensional spaces. In general, the spectral theorem will identify a class of MDR-TB linear operators that can be modeled by multiplication operators. In more abstract language, the spectral theorem is a statement about commutative C*-algebra.

In linear algebra, an orthonormal basis for an inner product space *V* with finite dimension is a basis for *V* whose vectors are orthonormal (Griffith 2003). For example, the standard basis for a Euclidean space $R^n$ is orthonormal in a robust spatiotemporal MDR-TB which would then represent a model where the relevant inner product would be the dot product of vectors. In mathematics, the dot product, or scalar product or sometimes inner product in the context of Euclidean space, is an algebraic operation that takes two equal-length sequences of numbers, usually coordinate vectors and returns a single number which then can be defined either algebraically or geometrically. The coordinate representation or coordinate vector of a vector is the unique tuple of numbers that describes the vector in terms of a particular ordered basis (Cressie 1993). Thus, the spatiotemporal-sampled clinical and environmental explanatory covariate coefficient coordinates would always be specified relative to an ordered basis. Bases and their associated coordinate representations would then enable realization of vector spaces and linear transformations concretely as column vectors, row vectors, and matrices, in the MDR-TB model . In three dimensional space the dot product would contrast with the cross product of two vectors, which then would produce a pseudovector as result in the model. A vector-like object which is invariant under inversion is called a pseudovector, or an axial vector (Hosmer and Lemeshew 2000). The cross product A × B is a pseudovector, whereas the vector triple product A× (B×C) is a polar vector. The term "polar vector" is used to refer to a representation of a vector magnitude (that is, length) and angle, which is equivalent to specifying endpoints (i.e., polar coordinates). In contrast, pseudovectors (i.e., axial vectors) do not reverse sign when the coordinate axes are reversed. Examples of polar vectors include the velocity vector, momentum, and force. The cross product of two polar vectors is a pseudo-vector (Cressie 1993). Polar vectors and pseudovectors are interrelated in the following ways under application of the cross product:

$$[\text{pseudovector}] \times [\text{pseudovector}] = [\text{pseudovector}]$$
$$[\text{vector}] \times [\text{pseudovector}] = [\text{vector}].$$

The dot product is directly related to the cosine of the angle between two vectors in Euclidean space of any number of dimensions (Cressie 1993).

Thus, the image of the standard basis under a rotation or reflection or any orthogonal transformation in the MDR-TB model then would also be orthonormal, and every orthonormal basis for $R^n$ would thus arise in a similar fashion. The natural basis for a polar coordinate system is orthogonal (Cressie 1993). Since For a general inner product space *V*, an orthonormal basis can be used to define normalized orthogonal coordinates on *V*, the inner product in the MDR-TB model would then become a dot product of vectors. Thus, the presence of an orthonormality in the model would reduce the study of a finite-dimensional inner product space to the study of $R^n$ under dot product. Further, since every finite-dimensional inner product space

space has an orthonormal basis (Griffith 2003), the MDR-TB distribution may be obtained from an arbitrary basis using the Gram–Schmidt process.

In mathematics, particularly linear algebra and numerical analysis, the Gram–Schmidt process is a method for orthonormalizing a set of vectors in an inner product space, most commonly the Euclidean space $R^n$. The Gram–Schmidt process takes a finite, linearly independent set $S = \{v_1, \ldots, v_k\}$ for $k \leq n$ and generates an orthogonal set $S' = \{u_1, \ldots, u_k\}$ that spans the same $k$-dimensional subspace of $R^n$ as $S$ (Cressie 1993). Unfortunately, certainty principles for orthonormal bases has not been spatially quantitated within a time series. As such, subspace sampling frame employing any form of relative-error matrix approximations for quantitating spatially dependent uncertainty has never been performed for an empirical dataset of MDR-TB explanatory clinical and environment covariate coefficients.

Additionally, violations of normality in a hierarchical linear spatiotemporal-sampled district-level MDR-TB model can also compromise the predictive estimation of clinical and/or environmental covariate coefficients and the calculation of confidence intervals. Generally, the error distribution in a time series-dependent MDR-TB infectious disease model is skewed by the presence of a few large outliers (Chatterjee and Hadi,1988). Scenes can calculate how symmetric the data is, in other words, if there a tendency for the data to be positive or negative (Fotheringham, 2002). Therefore, quantitating spatiotemporal MDR-TB regression-based covariates would simply require measuring the difference between the average and median of the sampled data (Smith, 1994; Johnston, 2003; Clarke et al., 2002; Akashi et al., 1996; Barr et al., 2000). The median measures the midpoint of the data, the value for which half the points are greater and half are smaller (Homser and Lemeshew, 2000).

Therefore, for a robust symmetrical MDR-TB distribution, like the normal, the median then would be the spatiotemporally tabulated averages and, as such, the quantitated skewness would be zero. Further, if the skewness is negative in the model then there would be more negative values indicating the presence of outliers. An outlying observation, or outlier, is one that appears to deviate markedly from other members of the sample in which it occurs and are often indicative either of measurement error, or that the population has a heavy-tailed distribution (Hosmer and Lemeshew, 2000; Manton and Stallard 1988). In probability theory, heavy-tailed distributions are distributions whose tails are not exponentially bounded: that is, they have heavier tails than the exponential distribution (Asmussen, 2003). If the skewness is positive in a spatiotemporal MDR-TB regression model then there are more positive values indicating the long tail generated by the explanatory covariate coefficients is on the positive side of the peak (i.e., "skewed to the right"). Spatiotemporal parameter estimation is based on the minimization of squared error; however, a few extreme observations can exert a disproportionate influence on sampled estimators (Griffith, 2003). For example, if the error distribution is significantly non-normal, in a time series-dependent MDR-TB regression-based model, the confidence intervals may be too wide or too narrow. Kurtosis is a measure of whether the data are peaked or flat relative to a normal distribution (Hosmer and Lemeshew 2000). Further, since kurtosis is a measure of the extreme observations in a spatiotemporal model (Hosmer and Lemeshew, 2000), the sign of skewness would also indicate if the sampled explanatory covariate coefficients was kurtotic.

Kurtosis is a descriptive statistics based on a relative concentration of scores in the center, the upper and lower ends (that is, tails), and the shoulders of a distribution (Fotheringham et al., 2002). As such, higher kurtosis in a spatiotemporal-sampled MDR-TB regression-based model constructed from an empirical dataset of clinical explanatory covariates coefficients for example, would indicate more of the variance in the residuals generated from the model was due to infrequent extreme deviations, as opposed to frequent modestly-sized deviations in the sampled covariate coefficients. Environmental-related data that has more kurtosis than the normal is sometimes called fat-tailed as its extremes extend beyond that of the normal (Piorecky and Prescott 2006, Wintle and Bardos 2006, Miller 2007, He et al. 2003,Hoeting et al. 2000). Ideally, a TB predictive risk modeler would prefer a distribution with low kurtosis (i.e., predictive residuals not far away from the mean). However, for spatiotemporal MDR-TB distribution to be normalized, the sampled explanatory covariate coefficients would have to exhibit an excess kurtosis equal to 0. Alternatively, a MDR-TB regression-based distribution with positive kurtosis in a spatiotemporal model would have to exhibit a peak in the middle and fat tails versus a normal distribution. Fat-tailed distributions have values of kurtosis that are greater than 3.0 (Fotheringham, 2002). Thus, the extreme values would be positive in a spatiotemporal MDR-TB regression–based model. However, this is only possible when the skewness in the model is positive. Further, the skewness is negative in the MDR-TB model combined with the impact of a high excess kurtosis would adversely affect causing extreme mispecified negative explanatory predictor covariate coefficient values in the residual error variance.

Frequently, adjusted version of Pearson's kurtosis has been used to quantitate the excess kurtosis and to provide a comparison of the shape of a given MDR-TB model distribution, to that of the normal distribution. Pearson (1905) introduced kurtosis as a measure of how flat the top of a symmetric distribution was when compared to a normal distribution of the same variance. He referred to more flat-topped distributions ($\gamma_2 < 0$) as "platykurtic," less flat-topped distributions ($\gamma_2 > 0$) as "leptokurtic," and equally flat-topped distributions as "mesokurtic" ($\gamma_2 \approx 0$).

Kurtosis is actually more influenced by scores in the tails of the distribution than scores in the center of a distribution (Hosmer and Lemeshew, 2000). Accordingly, it is often appropriate to describe a MDR-TB leptokurtic distribution as “fat in the tails” and a MDR-TB platykurtic distribution as “thin in the tails”. Distributions with negative or positive excess kurtosis are called leptokurtic distributions, respectively (Hosmer and Lemeshew, 2000). Leptokurtic distributions are identified by peaks that are thin and tall (Fotheringham 2002, 2000). Platykurtic curves, on the other hand, have shorter ‘tails’ than the normal curve of error and leptokurtic longer ‘tails’. Skewed distributions are always leptokurtic (Hopkins and Weeks, 1990). Pearson’s measure of kurtosis, however, has been often criticized as it does not focus adequately on the central part of a distribution. Although never proposed, an alternative measure of kurtosis for spatiotemporal MDR-TB regression-based modeling is one which adjusts the measurement of kurtosis by removing the effect of skewness using autocorrelation statistics.

Spatial autocorrelation is the correlation among values of a single variable strictly attributable to their relatively close locational positions on a two-dimensional surface, introducing a deviation from the independent observations assumption of classical statistics (Griffith, 2003). Since spatially structured infectious disease data always violate the assumption of independence (Legendre 1993), residual serial autocorrelation oriented statistics would enhance predictive autoregressive MDR-TB risk mapping based on sampled georeferenced explanatory covariate coefficients. Identification of the presence of positive autocorrelation (i.e., aggregation of similar values in geographic space) in residual predictive error variance-covariance matrices always leads to underestimation of standard errors and inflated Type I errors, when employing standard methods based on ordinary least squares (OLSs) (e.g. ANOVA, correlation, and regression) to test statistical hypotheses (Cliff and Ord, 1981; Legendre, 1993). Lennon (2000) argued that autocorrelation renders inflated Type I errors, and had a systematic bias towards particular predictive estimators with greater autocorrelation. These autocorrelation-related components may be illustrated by a density graph which can reveal the leptokurtic nature of a time series-dependent MDR-TB distribution rendered from a robust spatial autocorrelation matrix while simultaneously revealing the associated thicker tails compared to a normal density using an autocovariate term.

Traditionally, an autocovariate analysis is indexed with a Moran Coefficient (MC; a product moment correlation coefficient type of spatial autocorrelation index) (Griffith, 2002). The simplest and most straightforward null hypothesis, on which to test the significance of the MC, would assume spatial autocorrelation in an empirical spatiotemporal-sampled dataset of the MDR-TB-related explanatory covariate coefficients, for example, from which a sample is drawn to be zero. Two assumptions about the sample can then be made: the covariate coefficient values are drawn from a normally distributed population; or, the sample values represent one random arrangement of the attribute values from all the possible arrangements that could occur. MC indices may be tested using analytical expectations and variances from a non-linear estimation model based largely on the neighborhood structure assumed in a spatially weighted uncertainty-oriented matrix. The sampling distributions of MC rendered from a spatiotemporal MDR-TB regression-based model may then be quantitated as a dataset of asymptotically normally distributed standard errors of the estimators which may then be valid for summarizing virtually any type of non-normal factor analysis or, for certain structural equation model construction.

Further, recent quantitative geographical analysis methods have supplemented spatial statistics with an approach to quantify latent autocorrelation error coefficients, by decomposing the MC into synthetic variates whose linear combinations constitute a spatial filter model specification. This eigenvector filtering approach is a non-parametric technique that removes the inherent autocorrelation from generalized linear regression models by treating them as a missing variables (i.e., first order) effect. The aim of this non-parametric approach is to control spatial autocorrelation by introducing appropriate synthetic variables that serve as surrogates for serially correlated missing origins and destination variables (Griffith, 2003). This shift in focus leads to spatial filter variants of the classical spatial interaction model. Further, by so doing, the non-parametric spatial filtering may control for autocorrelation and heteroskedastic error components in a time-series dependent MDR-TB model with a set of spatial proxy predictor variables, rather than identify a global error autocorrelation parameter for a spatial process in the model. In time-series infectious disease models, heteroscedasticity (that is, uncommon variance) often arises due to the effects of inflation perhaps magnified by a multiplicative seasonal pattern (Griffith, 2005).The basis for this procedure is the decomposition the MC into orthogonal and uncorrelated map pattern components. As such, a MDR-TB-oriented spatial filter analyses can be used to account for an empirical dataset of regressed pseudo-replicated explanatory covariate coefficients by generating eigenvectors which may exhibit a distinct spatial topographic pattern while simultaneously rendering a given residual autocorrelation level.

The goal of this study was to identify geographic areas with on-going MDR-TB transmission in San Juan de Lurigancho (SJL), a district in Lima, Peru by performing a residual spatial autocorrelation analysis within an SAS database to derive simulation models. Our assumption was that the residuals from these models would reveal how departures from normality affect the performance of exact confidence intervals for a population mean and variance within a time series- dependent empirical

dataset of spatiotemporally-sampled clinical end environmental MDR-TB explanatory covariates. SAS PROC REG can calculate univariate statistics, and perform robust parsimonious linear and non-linear regression analyses using spatiotemporal-sampled data (www.sas.edu). In this research estimates generated from a global autocorrelation analyses were spatially decomposed into empirical orthogonal bases using a negative binomial regression with a non-homogeneous, gamma distributed mean. Thereafter, we proposed a test of goodness of fit for the time-series dependent models based on the sum of the squared residual partial autocorrelations. The test statistic was asymptotically $X^2$. The residual times-series autocorrelation estimation performance was thereafter studied through a Monte Carlo experiment. Monte Carlo experiments are a broad class of computational algorithms used in optimization and numerical intergration for generation of samples from a probability distribution (Cressie 1993). Another of our assumption in this research, was that the decomposition of Moran's coefficient into uncorrelated, MDR-TB orthogonal mapping components could reveal global spatial heterogeneities necessary to capture latent autocorrelation in a spatiotemporal regression-based model for implementing control strategies in the SJL study site.

Geographically based screening and treatment could be an effective method for MDR-TB control programs to identify high-risk populations (WHO, 2009).

In this research, we also complemented the autocovariate logistic parameter estimation model using a Bayesian Poisson matrix in SAS for formally hypothesis-testing the spatiotemporal-sampled MDR-TB drug resistant parameter estimators at the SJL study site. SAS/STAT software now provides Bayesian analysis including Bayesian zero-inflated Poisson models for zero-inflated count data employing a Markov Chain Monte Carlo (MCMC) algorithm in downloadable, experimental versions of three procedures for SAS 9.1.3 on Windows: GENMOD, LIFEREG, and PHREG (www.sas.edu). Markov Chain is a mathematical system that undergoes transitions from one state to another, between a finite or countable number of possible states which can be characterized as random "memoryless" process (Cressie 1993). In recent years MCMC has revolutionized the practicability of Bayesian inference methods allowing a wide range of posterior distributions to be simulated and their parameters to be quantitated numerically in time series-dependent infectious disease modeling. In Bayesian statistics, the posterior probability of a random event or an uncertain proposition in a time series dependent MDR-TB model would be the conditional probability that is assigned after the relevant evidence is taken into account (Cressie 1993). Similarly, the posterior probability distribution would be the MDR-TB distribution of an unknown quantity, treated as a random variable, conditional on the evidence obtained from an experiment or survey.

In this research specifically we used a Bayesian Poisson model to estimate the risks of resistance to four commonly used drugs at the SJL study site in TB treatment: isoniazid, rifampin, ethambutol, and streptomycin. A Bayesian Poisson vector autoregression model can characterize endogenous infectious disease dynamic count data with no restrictions on the contemporaneous correlations (Griffith, 2005). Bayesian linear regression techniques can also be used when the variance is assumed to be a function of the mean (Cressie, 1993). Therefore, it would be possible in some cases to amend the problem of propagated residual uncertainty in a time series dependent MDR-TB model by applying a transformation to the response variable (e.g., fitting the logarithm of the response variable using a linear regression model) which would then imply that the response variable has a log-normal distribution rather than a normal distribution. In probability theory, a log-normal distribution is a continuous probability distribution of a random variable whose logarithm is normally distributed (Hosmer and Lemeshew 2000).

Thus, if $X$ is a random variable in a spatiotemporal Bayesian generalized hierarchical MDR-TB spatiotemporal model with a normal distribution, then $Y = \exp(X)$ will have a log-normal distribution; likewise, if $Y$ is log-normally distributed in the model then $X = \log(Y)$ has a normal distribution. The log-normal distribution would then be the spatiotemporal MDR-TB model distribution of the sampled random variables with only positive real values.

Further, in this research, the decomposition of the residual forecast errors were illustrated in the Bayesian Poisson model residuals for quantitating the effects of exogenous covariate shocks. We then spatially decomposed uncertainty values to quantify the effects of exogenous-sampled explanatory covariate coefficients related to special resistant strains. Since drug resistance is very common in tuberculosis treatment (Orenstein et al., 2009), we assumed that robust Bayesian Poisson model outputs could quantitate interactions between the clinical and environmental sampled parameter estimators (i.e., resistant strain data) and time series-dependent MDR-TB district-level indices at the SJL study site. It is well known that drug resistance of TB is unevenly distributed and, therefore, MDR resistance can be perceived as problems of local rather than global importance (Dye et al., 2002). Although there have been a few studies on the mechanism of drug resistance in tuberculosis (Al-Orainey, 1989; Crofton et al., 1997), the reasons why tuberculosis is resistant to a certain treatment is largely unknown. Therefore, correctly estimating the drug resistance at a local level may have important implications for control and treatment of MDR-TB. As such, in this paper, we used a flexible Bayesian Poisson regression model to estimate the risk of drug resistance at the SJL study site. Further, since independent marginal distributions are necessary for non-

normal probability analyses in a predictive autoregressive risk model framework (Griffith 2003), we assumed that synthetic spatiotemporal MDR-TB map patterns based on specific disease transmission data (e.g., distribution of resistant strains) would produce robust pseudo-likelihood estimates with high predictive power.

In this paper we also considered both low and high-dimensional predictive residual uncertainty covariance matrix estimation problems and present asymptotic properties of sample MDR-TB -related covariances and covariance matrix estimates. In particular, we provide spatially quantitated asymptotic uncertainties for high dimensional covariance matrices in the time series, and a consistency result for the MDR-TB-related error covariance matrix estimation for regressing the spatiotemporal dataset of clinical and environmental explanatory covariate coefficients. The problem of high -dimensional covariance matrix latent error estimation often arises when estimate unknown parameters that are associated with a time series (Cressie 1993).

Additionally, we generated a residual Moran's coefficient (MC) minimization criterion for permitting a more detailed interpretation of latent autocorrelation in the MDR-TB data sampled at the SJL study site by allowing explicit visualization of inconspicuous negative spatial autocorrelation (NSA) patterns in the georef-erenced clinical and environmental parameter datasets. Negative spatial autocorrelation naturally materializes with competitive locational processes, negative spatial externalities, the spectrum (e.g., eigenvalues) of a geographic weights matrix, the calculation of linear regression residuals, and the computation of local indicator of spatial autocorrelation (LISA) statistics (Griffith, 2008; Anselin, 1995). To date spatial analyses of infectious disease data commonly have employed only a first conditional autoregressive model or, a second-order, that is, a simultaneous autoregressive with spatial lag covariance matrix for determining hidden NSA attributable to model misspecifications. Although these models have performed extremely well across a myriad of georeferenced attributes, higher order spatial covariance matrix specifications may be needed to capture NSA in an autoregressive spatiotemporal predictive risk MDR-TB model. Failure to posit the correct order of a spatial covariance matrix can constitute a prominent form of model error (Griffith, 2003). Thus, we assumed that qualitatively assessing residual time series dependent autocorrelation error coefficients may improve present MDR-TB control strategies at the SJL study site by revealing how hidden NSA furnishes a diagnostic in a predictive autoregressive risk model misspecification.

Since the prediction error is the expected quadratic loss incurred by the difference of observed event status and by the model predicted event probabilities (Cressie 1993), it may be shown that the prediction error is minimal in a MDR-TB if, and only if, the true probabilities are accurately spatially quantitated.

In this paper we considered both low and high-dimensional predictive residual uncertainty covariance matrix estimation problems and present asymptotic properties of sample MDR-TB-related covariances and covariance matrix estimates in GIS using QuickBird data. Raster representations of thematic and numerical spatial attributes of MDR-TB can be spatially quantitated in a GIS environment for computational simulation and analysis of spatial processes (Jacob et al. 2010). This paper addresses the problem of MDR-TB-related predictions and their uncertainty assessment for creating GIS raster representations created from a set of sample points of spatial attributes. Spatial mapping in GIS using sub-meter resolution remote sensing data [e.g., QuickBird visible and near infra-red (NIR) 0.61 m pixels] may be an alternative tool in MDR-TB control, in the SJL study site for aiding in the assessment of transmission dynamics for optimizing existing management programs. Accounting for the autocorrelation between neighboring districts, thereafter, and studying whether other spatiotemporal-sampled georeferenced district-level clinical and environmental covariate coefficients are related to drug resistance also may also develop and implement robust MDR-TB control strategies in the SJL study site. Therefore, our research objectives were: (1) to perform Poisson regression analyses to determine explanatory covariates affecting MDR-TB incidence rates; (2) to construct a flexible Bayesian regression model to esti-mate the risks of district-level resistance to four common drugs: rifampin, isoniazid, ethambutol and streptomycin; (3) to generate global autocorrelation statistics for evaluating spatial dependence and kurtosis among the data feature attributes while quantifying all residual error autocorrelation components in the model output; (4) to generate a Bayesian Poisson model for evaluating distri-bution of district-level resistant strains for identifying epicenters for MDR-TB and, (5) to use a Residual MC minimization criterion for detecting and quantitating non-conspicuous NSA in a dataset of clinical explanatory predictor variables spatiotemporally-sampled in SJL, Lima, Peru.

## MATERIALS AND METHODS

### Study Site

San Juan de Lurigancho (SJL) is the largest district in Lima, located in the Northeast area of the province of Lima. With a current population exceeding one million people, it is the country's most populous district, with a total surface area of 131.3 $km^2$ constituting 4.91% of the total area of the province of Lima. On the north, SJL is bordered by the districts of Carabayllo and San Antonio, which is in the Huarochirí Province. San Juan de Lurigancho is bordered by Comas, Independencia and Rímac on the west; and Lurigancho on the east. The Rímac River marks the district's border with downtown Lima and El Augustino on the south. The most important urban areas in the district are Mangomarca, Zárate, Las Flores, and Canto Grande and Bayovar. One of the first urban areas in SJL is Caja de Agua; which is located at the entrance of the district. Caja

de Agua is surrounded by San Cristobal and Santa Rosa hills from south to west. The altitude of SJL ranges from 2,240 meters above sea level (m.a.s.l.) at the peaks of Cerro Colorado Norte, to 200 m.a.s.l., at the level of the Rimac river. Urban areas have been developed in a longitudinal direction from the river border up to 350 m.a.s.l. The mean temperature ranges between 17 and 19ºC throughout the year.

**Subjects and setting**

This research used the data acquired from a retrospective study of a cohort of 1,571 patients diagnosed with pulmonary TB and MDR-TB enrolled over an 18 month period in the district of SJL in Lima, Peru.

**Patient selection and enrollment**

In this research all participating patients underwent a complete evaluation, including drug susceptibility for first line drugs. This was a prospective multi-center observational study comparing the use of several investigational techniques with standard methods to assess the *in vitro* antimicrobial susceptibility of *M. tuberculosis,* either directly from patient specimens or from culture isolates. One thousand two hundred and fifty adults with pulmonary tuberculosis cultures were confirmed with $\geq$10 colonies of *M. tuberculosis*. After collection of baseline samples and completion of initial measurements, including susceptibility testing by conventional and research methods, all subjects started anti-TB chemotherapy as dictated by the standard of care at the site of enrollment. Subjects were recruited, among patients presenting with smear positive pulmonary tuberculosis, to diagnostic and treatment sites in the following Health Centers: San Fernando, La Huayrona, Canto Grande, Jose Carlos Mariátegui, Huáscar XV, Huáscar II, Ganímedes, Cruz de Motupe, Piedra Liza, Bayóvar, Jaime Zubieta, San Juan, San Benito, Mangomarca, San Hilarion, Campoy, 15 de Enero, La Libertad, Juan Pablo II, Ascarruz Alto, 10 de Octubre, Sta Fe de Totoritas, Proyectos Especiales, Santa Rosa, Ayacucho, Zarate, Medalla Milagrosa, Campoy Alto, Montenegro, Santa Maria, Tupac Amaru II and Caja de Agua.

After confirmation of sputum smear microscopy results, subjects were screened for the presence of productive cough for eligibility in the study. Patients with positive sputum smear**s** are those with the capacity to spread infection (Godoy et al., 2004). Eligible subjects received an explanation of the study and were asked to provide written informed consent to participate. Initial data collected during screening included: a past medical history, collection of basic socio-demographic descriptors (age, sex, occupation, address, etc.) and a detailed symptom-oriented history with physical examination.

Drug susceptibility testing (isoniazid, rifampin, ethambutol and streptomycin) were performed by Gold Standard method on the initial sputum culture isolates of all enrolled subjects. Those subjects with initial drug resistant *M. tuberculosis* clinical isolates were determined using a treatment regimen with a duration deemed appropriate by a Committee of the National Tuberculosis Control Program (NTCP) and Committee for Evaluation of Retreatment (CER). All information collected was recorded on standardized data collection forms labeled with the date and the subject's name and study number, edited as needed and entered into data files for further analysis. Case report forms were then developed to record baseline clinical and socio-demographic data, HIV testing results, mycobacterial smear and culture results.

**Geographic mapping**

Field sampling was conducted from July 2005 to July 2007. Thirty-one Health Centers, in the study site, were mapped and classified using a CSI-Wireless differentially corrected global positioning systems (DGPS) Max receiver. This remote technology relies on the OmniStar L-Band satellite signal yielding a positional error of.179 m (± 0.392 m) (Jacob et al., 2007).

Data from the characterization of each epidemiological village was then recorded on a Mobile Vector Control Management System (VCMS™) electronic data recording device. The field sampling was extended to a 5 km distance from the external boundary of a sampled MDR-TB-related site. Specific environmental explanatory variables of the georeferenced data were recorded. Individual georeferenced Health Centers and their associated land cover attributes identified from the satellite imagery were then entered into a VCMS relational database software product. The VCMS database supported a mobile field data acquisition component module (Mobile VCMS) utilizing an industry standard Microsoft Windows Mobile™ device and an add-on DGPS connection. In this research, Mobile VCMS™ and its FieldBridge Server middleware component were used to support wireless synchronization of the clinical and environmental MDR-TB data collected at the SJL study site directly into a centralized database repository. Additional geocoding and spatial display of the clinical and environmental sampled data was handled in the embedded VCMS GIS Interface Kit™. This was developed using ESRI's MapObjects™ 2 technology. The VCMS database with the DGPS information, supported exporting all data in a spatial format; whereby, any individual Heath Center data and supporting MDR-TB covariates were described in an ESRI shapefile format for use in GIS. The database displayed this information on a user-defined field base map.

**Remote sensing data**

QuickBird (www.digitalglobe.com) images were acquired in March 11th 2008 for the SJL study site. QuickBird multispectral products provided four discrete non-overlapping spectral bands covering a range from 0.45 to 0.72 µm, with an 11-bit collected information depth with a spatial resolution of 0.61 m (Figure 1)

The QuickBird imagery was then classified using the Iterative Self-Organizing Data Analysis Technique (ISODATA) unsupervised routine in ERDAS *Imagine* v.8.7™. The images were co-registered manually, using gathered ground control point (GCPs) and georectified images from the QuickBird data. The satellite images were co-registered by applying a first order polynomial algorithm with a nearest neighbor resampling method and the GCPs.. The Universal Transverse Mercator (UTM) Zone 37S datum WGS-84 projection was used for all of the spatial datasets.

**Environmental parameters**

Variables recorded included, MDR-TB prevalence rates, distance between individual Health Centers, population data, and aspects of catchment-related ecohydrological land-surface covariates in the SJL study site such as elevation and slope per sampled site. Distance measures were recorded in ArcGIS 9.2® with QuickBird data and by field sampling. The distance between Health centers was categorized into numerous classes (e.g., 1: 0 to 5 km; 2: 5 to 10 km, and so on). The number of individuals cases of MDR-TB at each individual Health Center was then calculated and recorded (Table 1).

**Regression analyses**

All sampled parameters were entered in Excel files and analyzed using SAS 9.1.3® (SAS Inc. Cary, North Carolina). The first stage of

**Figure 1.** QuickBird visible and near infra-red data of the San Juan de Lurigancho study site.

**Table 1.** Clinical and environmental MDR-TB data sampled in the San Juan de Lurigancho study site.

| Variable in database | Description of variable |
|---|---|
| ESTAB | Health care center |
| FENAC | Birth date |
| EdadA | Age |
| SEXO | Sex |
| TIPOVIV | Home |
| NUMHAB | Number of bedrooms |
| MATVIV | Building material |
| NUMPER | Number of persons living in the house |
| ELECTRIC | Electricity supply at home |
| AGUAPOT | Home access to potable water |
| DESAGUE | Wastepipe connected to the public network |
| ECIVIL | Marital status |
| OCUPA | Ocupation |
| TRAESTS | Do you work in any health care center? |
| TIEMTRA | Time of employment |
| INGMEN | Salary/Income per month |
| LJINH | Sensitivity test to isoniazid in LJ medium |
| LJIRIF | Sensitivity test to rifampin in LJ medium |
| LJIETB | Sensitivity test to ethambutol in LJ medium |
| LJISTM | Sensitivity test to streptomycin in LJ medium |
| MDR | Multidrug resistant |

this analysis utilized Poisson regression to determine the relationship between the MDR-TB sampled clinical and environmental covariates. Poisson regression is one special case of the Generalized Linear Model (GLM) which allows one to fit models to a dependent variable that is a member of the exponential distribution family for linear quantitation of covariate variabilities. (Pielou, 1969). Our MDR-TB GLM was characterized with three components: the distribution of the dependent variable, a linear function of a set of

independent variables, and a link function between the dependent variable and its expectation as expressed by the linear function of independent variables. When the logarithm was applied as a link function, the Poisson regression had a log-linear form. Poisson regression is estimated based on the likelihood function that is constructed under the independence assumption (Haight 1967). Poisson distribution predicts non-negative integers in data analyses, where the mean and variance are equal (Kaiser and Cressie, 1997).

Next, non-linearity in the relationship between MDR-TB resistant infection rates and their explanatory predictor variables, were explored by adding polynomial terms and then grouping the values of continuous variables into categorical ones. Variable selection for the multiple regression models was carried out by a combination of automatic (stepwise) procedures and goodness-of-fit criteria and by selecting the covariates that explained the prevalence of MDR-TB cases and distribution in the SJL study site. A Poisson regression with statistical significance, determined by a 95% confidence level was then constructed to ascertain whether the proportions of sampled explanatory predictor variables differed by individual MDR-TB Health Centers.

The Poisson regression assumed that each independent count value (that is. $n_i$), recorded at a Health Center location $i$=1,2,…$n$, from a sampled covariate was from a Poisson distribution. These data were described by a set of predictor variables denoted by matrix $\mathbf{X}_i$, a 1×$p$ vector of covariate values for a Health Center location $i$. The expected value of these data was given by $\mu_i(\mathbf{X}_i)=n_i(\mathbf{X}_i)\exp(\mathbf{X}_i\boldsymbol{\beta})$, where $\boldsymbol{\beta}$ was the vector of non-redundant parameters, and the Poisson rates parameter was given by $\lambda_i(\mathbf{X}_i)=\mu_i(\mathbf{X}_i)/n_i(\mathbf{X}_i)$; the rates parameter $\lambda_i(\mathbf{X}_i)$ was both the mean and the variance of the Poisson distribution as in McCullagh and Nelder, (1989) for sampled Health Center location $i$. The regression analyses were performed in SAS PROCREG. The sampled data was log-transformed before analyses to normalize the distribution and minimize standard error.

Thereafter, we used a Bayesian Poisson model to estimate the risks of resistance to each of the four common drugs in TB treatment. We then fit a Bayesian Poisson regression model for the frequency of the strains with density using MDR-TB$i$ $\text{Poisson}(\lambda_i)\log(\lambda_i)=\mathbf{X}_i\boldsymbol{\beta}$ (2.1) for the $i=1,\ldots,18$ plates, where $\boldsymbol{\beta}$ represented the regression parameters and $\mathbf{X}_i$ was the vector of covariates The likelihood function for each of the corresponding MDR-TB sampled explanatory covariates was $p(\text{SMDR}/\mathbf{X}_i\boldsymbol{\beta}=\text{Poisson}(\lambda_i)$ where $p(\cdot|\cdot)$denoted a conditional probability mass function. The Poisson density was then evaluated with a corresponding mean parameter $\lambda_i$. The three parameters, $\beta_1$, $\beta_2$, and $\beta_3$, corresponded to an intercept, the positive and the negative effect of the strain respectively. The following prior distributions were then placed on the spatiotemporal-sampled MDR-TB parameter estimators, where $\pi(\cdot)$ indicated a prior distribution: $\pi(\beta_1),\pi(\beta_2),\pi(\beta_3)=\text{normal}(0,\sigma^2=1000)$. The diffuse $\text{normal}$ prior expressed lack of knowledge about the regression parameters.

Using Bayes' theorem, the likelihood function and prior distributions determined the posterior distribution of $\beta_1,\beta_2$, and $\beta_3$. The goodness-of-fit Pearson chi-square statistic $\chi^2_P$ was then derived as in McCullagh and Nelder (1989).By so doing we were able to assess model fit which in this research was achieved employing MDR-TB$i$-E(MDR$i$)]$^2$:/ V (MDR-TB$i$). We let $E(\cdot)$ represent an expectation for a Poisson likelihood E(MDR-TB$i$= V( MDR-TB$i$) where $\lambda_i$ was defined in Equation 2.1 If there is no overdispersion, the Pearson statistic approximately equals the number of observations in the data set minus the number of parameters in the model.(Fotheringjam 2002)

The parameter $\mu$ was interpreted as rates (e.g., the average number of new TB cases per 1,000 population). If $Y$ is the number of occurrences, its probability distribution can be written as:

$$f(y)=\frac{\mu^y e^{-\mu}}{y!},$$

for $y=0,1,2,\ldots$

where $\mu$ was the mean number of occurrences (Kaiser and Cressie, 1997). We then used $y_i$ to denote the number of MDR-TB patients who were resistant to a specific drug in a georeferenced health center $i$. We let $Ni$ denote the population size of health center $i$. We assumed a Poisson model for the spatial count data as follows:

$$\sim(a\,bi)$$

$$i\,i\,y\,Poisson\,N\,e+,i=1,2,\ldots,M.$$

where

$i\,b$

was the spatial random effect for the $i$th georeferenced health center, controlling whether the risk is above or below the average.

We further modeled the spatial random effect $b_i$ using a conditionally autoregressive (CAR) prior (see Hodges et al., 2003). In this research under the CAR prior,

$$b_i \sim N\left(\frac{\sum_{j\in\partial_i} b_j}{m_j},\frac{\sigma^2}{m_j}\right), \quad i=1,2,\ldots,M.$$

where $\partial_i$ was the index set of neighboring districts of the $i^{\text{th}}$ district, $m_j$ was the number of neighboring districts to the district $i$, and $\sigma^2$ was the unknown variance parameter. We used noninformative priors for other assessing additional parameter estimators which were represented as a flat prior for N and a conjugate inverse gamma prior for $\sigma^2$. In Bayesian probability theory, the posterior distributions $p(\theta|x)$ are in the same family as the prior probability distribution $p(\theta)$. Thereafter, the prior and posterior were the conjugate distributions, and the prior was a conjugate prior for the likelihood in the MDR-TB model.

The Gaussian family is conjugate to itself (that is, *self-conjugate*) with respect to a Gaussian likelihood function in a spatiotemporal model if the likelihood function is Gaussian, (Fotheringham 2002). In this research, choosing a Gaussian prior over the mean ensured that the posterior distribution was also Gaussian. Further, the Gaussian distribution was a conjugate prior for the likelihood which was also Gaussian in the model. Conjugate priors are analogous to eigenfunctions in operator theory, in that they are distributions on which the "conditioning operator" acts in a well-understood way, thinking of the process of changing from the prior to the posterior as an operator.

**Spatial analyses of MDR-TB covariates using Moran's *I***

Spatial autocorrelation was evaluated among the sampled clinical and environmental covariates at the SJL study site using Moran's *I*. In statistics, Moran's *I* is a measure of spatial autocorrelation (Griffith, 2003) In this research Moran's *I* was defined as

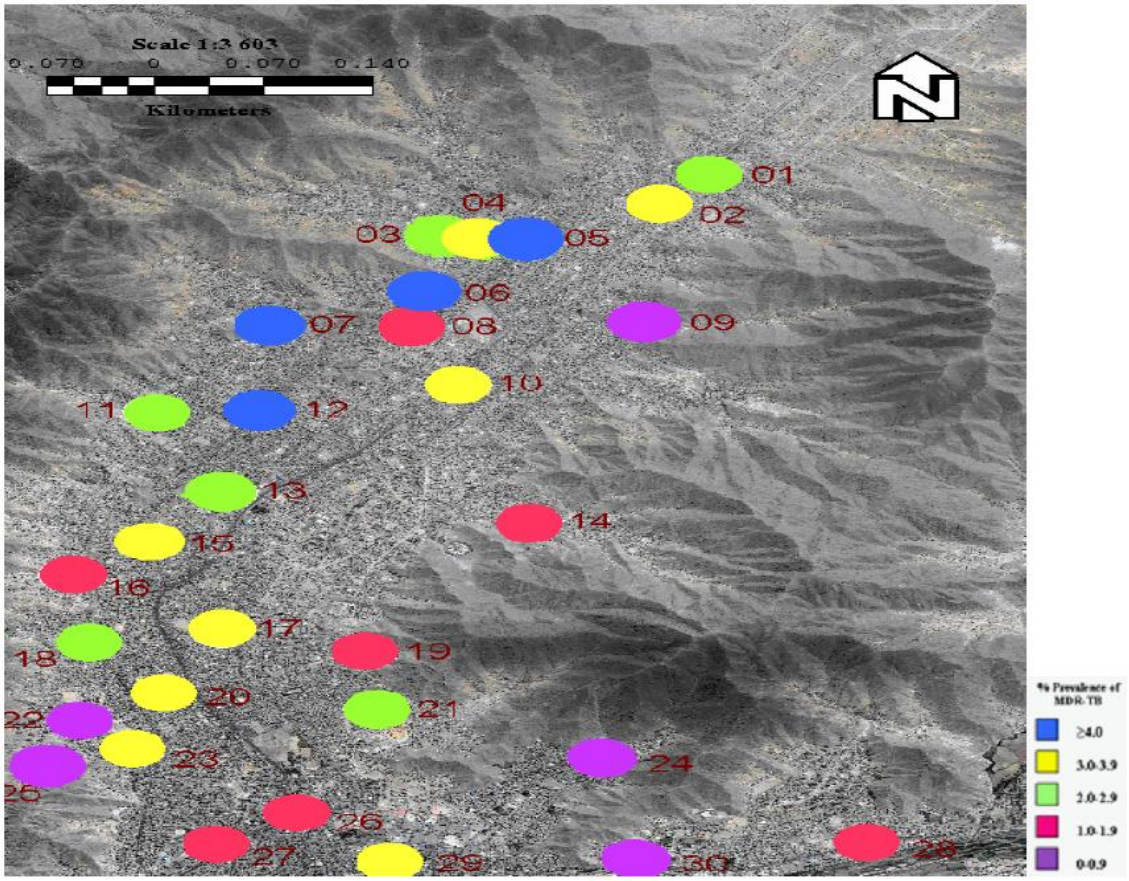


**Figure 2.** Geographical clusters of Health Centers in San Juan de Lurigancho study site.

$$I = \frac{N}{\sum_i \sum_j w_{ij}} \frac{\sum_i \sum_j w_{ij}(X_i - \bar{X})(X_j - \bar{X})}{\sum_i (X_i - \bar{X})^2}$$

where $N$ was the number of georeferenced health centers indexed by $i$ and $j$; $X$ was the MDR-TB incidence rates; $\bar{X}$ was the mean of $X$; and $w_{ij}$ was an element of a matrix of spatial weights. The expected value of Moran's *I* under the null hypothesis of no spatial autocorrelation was then:

$$E(I) = \frac{-1}{N-1}$$. Its variance thereafter was equal to:

$$Var(I) = \frac{NS_4 - S_3 S_5}{(N-1)(N-2)(N-3)(\sum_i \sum_j w_{ij})^2}$$

Where

$$S_1 = \frac{1}{2} \sum_i \sum_j (w_{ij} + w_{ji})^2$$

$$S_2 = \frac{\sum_i (\sum_j w_{ij} + \sum_j w_{ji})^2}{1}$$

$$S_3 = \frac{N^{-1} \sum_i (x_i - \bar{x})^4}{(N^{-1} \sum_i (x_i - \bar{x})^2)^2}$$

$$S_4 = \frac{(N^2 - 3N + 3)S_1 - NS_2 + 3(\sum_i \sum_j w_{ij})^2}{1}$$

$$S_5 = S_1 - 2NS_1 + \frac{6(\sum_i \sum_j w_{ij})^2}{1}$$

For statistical hypothesis testing, the Moran's *I* values were then transformed to *Z*-scores where values greater than 1.96 or smaller than −1.96 indicated spatial autocorrelation that was significant at the 5% level.

We also used the Geary's coefficient (that is, Geary's C) which is inversely related to Moran's *I*,. Moran's *I* is a measure of global spatial autocorrelation, while Geary's C is more sensitive to local spatial autocorrelation (Griffith, 2003). In this research Geary's C was defined as

$$C = \frac{(N-1) \sum_i \sum_j w_{ij}(X_i - X_j)^2}{2W \sum_i (X_i - \bar{X})^2}$$

where $N$ was the number of health centers indexed by $i$ and $j$; $X$ where the MDR-TB incidence rates ; $\bar{X}$ was the mean of $X$; $w_{ij}$ was a matrix of spatial weights; and $W$ was the sum of all $w_{ij}$. The value of Geary's C lies between 0 and 2. Geary's C is inversely related to Moran's *I*, but it is not identical (Cliff and Ord 1971). Moran's *I* is a measure of global spatial autocorrelation, while Geary's C is more sensitive to local spatial autocorrelation (Griffith, 2003). Neighboring georeferenced health centers were then identified based on MDR-TB resistant prevalence values (Figure 2)

We analyzed the *n*-by-1 vector $x = [x_1 \cdots x_n]^T$ containing the MDR-TB covariates for *n* spatial units and n-by-n symmetric spatial weighting matrix W using Moran's Indices. The usual formulation for Moran's index of spatial autocorrelation (Griffith, 2003) is

$$I(x) = \frac{n\sum_{(2)} w_{ij}(x_i - \bar{x})(x_j - \bar{x})}{\sum_{(2)} w_{ij}\sum_{i=1}^{n}(x_i - \bar{x})^2} \quad (1)$$

The values $w_{ij}$ where the spatial weights based on the sampled clinical and environmental MDR-TB variables stored in the matrix **W** where $\sum_{(2)} = \sum_{i=1}^{n}\sum_{j=1}^{n}$ with $i \neq j$ which had a null diagonal $(w_{ii} = 0)$. This symmetric matrix revealed W*ij* = W*ji* was then generalized to a non-symmetric matrix W by using W=(W*+W*T/2) .

Moran's *I* was then rewritten using matrix notation as:

$$I(x) = \frac{n}{1^t W 1}\frac{x^T HHWHHx}{x^T HHx} = \frac{n}{1^T W 1}\frac{x^T HWHx}{x^T Hx} \quad (2)$$

SAS/GIS® (http://www.sas.com/products/gis/) was then used to perform the spatial filter analysis on the sampled MDR-TB data while SAS PROC GENMOD was used to build Poisson models with a gamma-distributed mean. In the study site, positive spatial autocorrelation (PSA) and NSA eigenvectors were selected by the stepwise negative binomial regression procedure. To expand the inferential basis with a random effect, a GLMM was used to account for latent non-spatial residual correlation time series dependent MDR-TB data. The GLMM estimation was computed using SAS PROC NLMIXED.

**Spatial eigenvector mapping**

Global indicators of spatial autocorrelation were then calculated from the ground-based and remotely-sensed ecological databases. Box-Cox type of power transformation was employed for normal approximation analysis purposes so that the frequency distributions of the georeferenced Health Centers in the SJL study site better approximated a bell-shaped curve. The spatial filter construction methodology transformation procedure was then used, as proposed by Griffith (2003), which depended on the eigenfunctions of a spatially weighted matrix.

To identify spatial clusters that can be uncovered with spatial filtering, Thiessen polygon surface partitionings were generated to construct geographic neighbor matrices, each denoted by the spatially weighted matrix which also was used in the spatial autocorrelation analysis. Entries in matrix were 1, if two health centers shared a common Thiessen polygon boundary and 0 otherwise. Next, the linkage structure for each surface was edited to remove unlikely geographic neighbors to identify pairs of health centers sharing a common Thiessen polygon boundary (Liang and Zeger, 1986; Griffith and Peres-Neto, 2006; Pielou, 1969; McCullagh and Nelder, 1989; Fotheringham, 1993; Wintle and, Bardos 2006). Eigenvectors of a modified version of the spatially weighted matrix was then used to furnish synthetic variates to determine distinct MDR-TB map patterns representing the full range of autocorrelation possibilities. Attention was restricted to those map patterns associated with at least a minimum level of spatial autocorrelation, which, for implementation purposes, was defined by $|MC_j/MC_{max}| > 0.25$, where $MC_j$ denoted the *j*th value and $MC_{max}$, the maximum value of MC. This threshold value allowed two candidate sets of eigenvectors to be considered for substantial positive and substantial negative spatial autocorrelation respectively.

Extending the findings of de Jong et al. (1984) and Tiefelsdorf and Boots (1995) we established a set of MC values that was related to matrix (**I** _ **11**T/*n*)**C**(**I** _ **11**T/*n*), where **C** was a 0/1 binary geographic connectivity weights matrix, **I** was an *n*-by-*n* identity matrix, **1** was an *n*-by-1 vector of ones, T was the matrix transpose, and, vector **Y** was the pre-multiplied georeferenced data matrix (**I** _ **11**T/*n*). In practice, these MC values are related to the binary geographic connectivity matrix **C** itself, after the principal eigenvalue has been replaced with 0 (Griffith and Amrhein, 1997). The decomposition discussed by Tiefelsdorf and Boots furnished a basis for the eigenfunction decomposition approach outlined here. In this research the decomposition expressed a given MI value as a weighted sum of the eigenvalues of matrix (**I** _ **11**T/*n*)**C**(**I** _ **11**T/*n*). Additionally, our model revealed that the upper and lower bounds for the spatial matrix generated using MC was rendered by $\lambda_{\max}(n/1^T W 1)$ and $\lambda_{\min}(n/1^T W 1)$ where $\lambda_{\max}$ and $\lambda_{\min}$ which were the extreme eigenvalues of $\Omega = HWH$. Hence, in this research, the eigenvectors of $\Omega$ were vectors with unit norm maximizing MC. The eigenvalues of this matrix were equal to MC of spatial autocorrelation post-multiplied by a constant. Eigenvectors associated with high positive (or negative) eigenvalues have high positive (or negative) autocorrelation (Griffith, 2003).

The diagonalization of the spatial weighted matrix generated from the clinical and environmental-sampled MDR-TB explanatory covariates coefficients consisted of finding the normalized vectors , stored as columns in the matrix $U = [u_1 \cdots u_n]$, which satisfied: $\Omega = HWH = U\Lambda U^T = \sum_{i=1}^{n}\lambda_i u_i u_i^T$ where $\Lambda = diag(\lambda_1 \cdots \lambda_n)$, $u_i^T u_i = \|u_i\|^2 = 1$ and $u_i^T u_j = 0$ for $i \neq j$ (Griffith, 2003). The double centering of $\Omega$ implied that the eigenvectors $u_i$ generated from the sampled MDR-TB covariates were centered and that at least one eigenvalue was equal to zero. Introducing these eigenvectors in the original formulation of MC led to:

$$I(x) = \frac{n}{1^T W 1}\frac{x^T HWHx}{x^T Hx} = \frac{n}{1^T W 1}\frac{x^T U\Lambda U^T x}{x^T Hx} = \frac{n}{1^T W 1}\frac{\sum_{i=1}^{n}\lambda_i x^T u_i u_i^T x}{x^T Hx} \quad (3)$$

Considering the centered vector $z = Hx$ and using the properties of idempotence of $H$, Equation (2.3) was equivalent to:

$$I(x)=\frac{n}{1^TW1}\frac{\sum_{i=1}^{n}\lambda_i z^T u_i u_i^T z}{z^T z}=\frac{n}{1^TW1}\frac{\sum_{i=1}^{n}\lambda_i \left\|u_i^T z\right\|^2}{\left\|z\right\|^2} \quad (4)$$

As the eigenvectors $u_i$ generated from the eigendecomposition of the spatially weighted matrix and the vector $z$ were centered, Equation (2.4) was then rewritten as:

$$I(x)=\frac{n}{1^TW1}\frac{\sum_{i=1}^{n}\lambda_i cor^2(u_i,z)\mathrm{var}(z)n}{\mathrm{var}(z)n}=\frac{n}{1^TW1}\sum_{i=1}^{n}\lambda_i cor^2(u_i,z) \quad (5)$$

In this research $r$ was the number of null eigenvalues of $\Omega(r\geq 1)$. These eigenvalues and corresponding eigenvectors were removed from $\Lambda$ and $U$ respectively. Equation (2.5) was then equivalent to:

$$I(x)=\frac{n}{1^TW1}\sum_{i=1}^{n-r}\lambda_i cor^2(u_i,z) \quad (6)$$

Moreover it was demonstrated that MC for a given eigenvector $u_i$ generated from the clinical and environmental sampled MDR-TB covariates was equal to $I(u_i)=(n/1^TW1)\lambda_i$ so the equation was rewritten:

$$I(x)=\sum_{i=1}^{n-r}I(u_i)cor^2(u_i,z) \quad (7)$$

The term $cor^2(u_i,z)$ represented the part of the variance of $z$ that was explained by $u_i$ in the spatiotemporal MDR-TB model using $z=\beta_i u_i+\varepsilon_i$. Estimation of covariance matrices is needed in the construction of confidence regions for unknown parameters, hypothesis testing, principal component analysis, prediction, discriminant analysis among others (Cressie 1993).This quantity was equal to $\beta_i^2/n\,\mathrm{var}(z)$. By definition the eigenvectors $u_i$ were orthogonal and therefore regression coefficients of the MDR-TB model was verified employing $z=\beta_i u_i+\varepsilon_i$ were those of the multiple regression model were quantified by $z=U\beta+\varepsilon=\beta_i u_i+\cdots+\beta_{n-r}u_{n-r}+\varepsilon$.

The distribution of the error residuals in the autocovariance matrix of the spatiotemporal MDR-TB was then quantified**.** The maximum value of $I$ was obtained by all of the variation of $z$ as explained by the eigenvector $u_1$ which corresponded to the highest eigenvalue $\lambda_1$ in the autocorrelation error matrix. In this research, $cor^2(u_i,z)=1$ (and $cor^2(u_i,z)=0$ for $i\neq 1$) and the maximum value of $I$, was deduced for Equation (2.7), which was equal to $I_{\max}=\lambda_1(n/1^TW1)$. The minimum value of $I$ in the error matrix was obtained as all the variation of, $z$ was explained by the eigenvector $u_{n-r}$ corresponding to the lowest eigenvalue $\lambda_{n-r}$ rendered from the MDR-TB model. This minimum value was equal to $I_{\min}=\lambda_{n-r}(n/1^TW1)$. If the clinical and environmental sampled predictor variable was not spatialized, the part of the variance explained by each eigenvector was equal, on average, to $cor^2(u_i,z)=1/n-1$. Because the clinical and environmental-sampled MDR-TB explanatory covariates in $z$ were randomly permuted, it was assumed that we would obtain this result. In this research the set of $n!$ random permutations, revealed that

$$\mathrm{E}_R(I)=\frac{n}{1^TW1(n-1)}\sum_{i=1}^{n}\lambda_i=\frac{n}{1^TW1(n-1)}trace(\Omega)$$

It was easily demonstrated that $trace(\Omega)=-\frac{1^TW1}{n}$ and it followed that $\mathrm{E}_R(I)=-\frac{1}{n-1}$.

We also used a Residual MC Minimization criterion suggested by van Tiefelsdorf and Griffith (2007) to further decompose the MC generated from the spatial decomposition of the sampled MDR-TB predictor variables to detect hidden NSA in the clinical and environmental data. The MC expected value for residuals from a linear spatial filter analyses was constructed with the eigenvectors from the MDR-TB data analyses using:

$$-\frac{n}{1^TC1}\frac{TR\left[\left(X^TX\right)^{-1}X^TCX\right]}{n-P-1}=\frac{n}{1^TC1}\frac{TR\left\{\left[(1E_P)^T(1E_P)\right]^{-1}(1E_P)^TC(1E_P)^T\right\}}{n-P-1}$$

$$=\frac{n}{1^TC1}\frac{1^TC1/n+\sum_{j=1}^{P}\lambda_j}{n-P-1}$$

$$=\frac{n}{1^TC1}\frac{1^TC1/n+\sum_{j=1}^{H}\lambda_j}{n-P-1}-\frac{n}{1^TC1}\frac{\sum_{j=H+1}^{K}\lambda_j}{n-P-1}+\frac{n}{1^TC1}\frac{\sum_{j=K+1}^{P}\lambda_j}{n-P-1} \quad (2.8)$$

where X=1E*p* was a covariate matrix, 1 was an n-by-1 vector of ones, **C** was the binary geographic weights connectivity matrix when , c*ij* = 1 but only if, georeferenced health centers *i* and *j* were adjacent, and c*ij* = 0 otherwise; $\mathbf{1}^T\mathbf{C1}$ counted the number of ones in the spatially weights matrix, **T** denoted matrix transpose, **TR** denoted the matrix trace operator, $\mathbf{E}_p$ was the *n*-by-P matrix of selected eigenvectors, *kj* was the eigenvalue corresponding to the *j*th eigenvector appearing in the SF $\left(MC_i=\frac{n}{1^TC1}\lambda_j\right)$; H was the number of selected eigenvectors portraying PSA, *K – (H* + 1*)* were the number of selected eigenvectors classified as compensatory and P – K were the number of selected eigenvectors portraying NSA in the MDR-TB model residuals generated from the spatial filter analyses. The right-hand side of Equation 2.8 then contained three terms. The first represented the expected value of MC for the PSA uncovered with the restricted candidate set of PSA eigenvectors; the second represented the expected value of MC for the additional PSA eigenvectors selected to counterbalance selection of NSA eigenvectors; and, the third represented the expected value of MC for the eigenvectors capturing hidden NSA. Equation 2.9 then indicated that when the residual MC value was positive and a hidden NSA spatial filter moved the corresponding residual MC expected value back toward zero, but at a rate

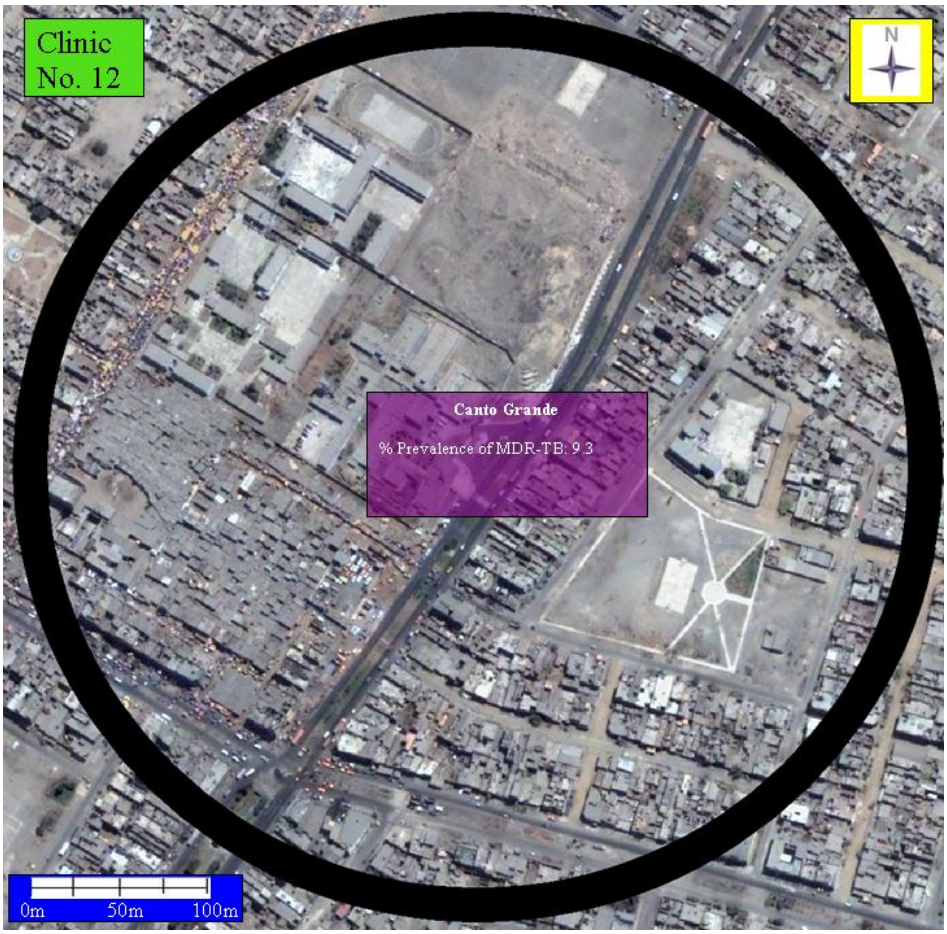


**Figure 3.** 1 km grid-based algorithm for Canto Grande Health Center with display of MDR-TB prevalence rate.

discounted by the denominator adjustment (that is, the additional subtraction of P – K). Meanwhile, the residual MC for a spatial filter was given by:

$$MC_Y - MC_{\hat{Y}} = MC_Y - \frac{n}{1^T C 1} \frac{\sum_{j=1}^{P} b_j^2 \lambda_j}{\sum_{j=1}^{P} b_j^2} \quad (9)$$

where $MC_Y$ denoted the MC for the georeferenced response variable **Y,** $MC_{\hat{Y}}$ denoted the MC for a constructed spatial filter, and *bj* denoted the linear regression coefficient of the *j*th eigenvector.

In this research all spatially filtered MDR-TB data in SAS/GIS® were integrated with SAS® application, using SAS/EIS. SAS/GIS® allowed for the creation and modification of the MDR-TB maps, as well as interactive feature selection and exploration. Typically, SAS/GIS® application sessions, driven from SAS/EIS®or SAS/AF®, provide powerful SAS Component Language (SCL) components and data step processing capabilities for manipulating data, such as theme datasets utilized in disease mapping (Jacob et al. 2010a). The SAS/GIS® module allowed for the creation and modification of the MDR-TB maps to accurately display results, as well as interactive feature selection and exploration of each georeferenced health center. Spatial information, of each individual health center was imported interactively and in a batch mode.

Additionally**,** Proc MAPIMPORT was used to import the shapefile data created from the MDR-TB data into a SAS/Graph as map datasets. The geographic tables generated, however, had to be processed to identify the coordinates of each health center, with attribute tables being joined to the sampled MDR-TB explanatory covariates for statistical analyses and cartographic display. Additionally, the SAS/GIS® program action linked each table generated with a subset of key predictor variables associated to each sampled Health Center. Thematic map layers were then used to provide more detail for each table. In this research SAS/GIS® used SAS/SHARE to open all datasets, allowing GIS applications to simultaneously read and update all data generated.

## RESULTS

A grid-based algorithm and a 1 km buffer generated in an ArcGIS® geodatabase, overlaid on the QuickBird visible and NIR data identified all health centers in the SJL study site. Each grid cell within the matrix contained an attribute value (MDR-TB covariate coefficient value), as well as location coordinates. The spatial location of each cell was implicitly contained within the ordering of the matrix. The health center with the highest MDR-TB prevalence rate was Canto Grande (9.3), while the lowest

**Table 2.** Global spatial analyses of MDR-TB prevalence rates by Health Centers in the San Lurigancho study site.

| Study site | n | Transformation | MC | $s_{MC}$ | GR |
|---|---|---|---|---|---|
| San Lurigancho | 120 | LN(count + 1.5) | 0.58 | 0.06 | 0.81 |

LN, Natural logarithm; MC, Moran coefficient; $s_{MC}$, the standard error of the MC; GR, geary ratio.

**Table 3.** Poisson spatial filtering model results for MDR-TB prevalence rates by Health Centers in the San Lurigancho study site.

| Spatial statistics | Model output |
|---|---|
| SF: No. of eigenvectors | 7 |
| SF: MC | 0.03 |
| SF: GR | 0.68 |
| SF pseudo-$R^2$ | 0.32 |
| Positive SA SF: No. of eigenvectors | 2 |
| Positive SA SF: MC | .899 |
| Positive SA SF: GR | 0.06 |
| Positive SA SF pseudo-$R^2$ | 0.04 |
| Negative SA SF: No. of eigenvectors | 3 |
| Negative SA SF: MC | -0.48 |
| Negative SA SF: GR | 0.63 |
| Negative SA SF pseudo-$R^2$ | 0.29 |
| Deviance statistic | 1.03 |
| Dispersion parameter | 0.11 |

MC, Moran's coefficient; GR, Geary's ratio; SF, spatial filter; SA, spatial autocorrelation; A pseudo-$R^2$ is the squared correlation between observed and GLM-predicted counts.

**Table 4.** Poisson spatial filter (SF) generalized linear mixed model (GLMM) random effects for MDR-TB prevalence rates by Health Centers in the San Lurigancho study site

| Statistics | Model ouput |
|---|---|
| Mean | 0.03 |
| Standard deviation | 0.31 |
| MC | 0.14 |
| GR | 0.78 |
| Pseudo-$R^2$ | 0.86 |
| Changes in significance (using a 0.10 level) of eigenvectors | none |

MC, the Moran coefficient; GR, the geary ratio; SA, spatial autocorrelation.

MDR-TB resistant rate was Campoy Altos (0.5) (Figure 3).

An examination of the model output from the Poisson regression analyses indicated that significant over-dispersion was present in the sampled MDR-TB data. Therefore, a negative binomial was used to model the overdispersed Poisson data. Negative binomial regression models estimate a dispersion parameter that can be used to remove the effects of overdispersion and provide more accurate estimates of standard error (Kaiser and Cressie, 1997). The negative binomial was derived as a Poisson–gamma mixture and as a GLM. PROC GENMOD expresses the variance of the response for the negative binomial as variance($y$) = μ + $k$μ2, as opposed to the more common notation, ($y$) = μ + μ2/$v$μ (Pielou, 1969). In this research the difference in notation was trivial ($k$ = 1/$v$).

The straightforward derivation of the linear MDR-TB model, from the negative binomial probability distribution function, did not, equate with the Poisson–gamma mixture-based version of the negative binomial. Rather, canonical link and inverse canonical link were converted to log form. A GLM-based negative binomial was produced that yielded identical parameter estimates based on the sampled MDR-TB covariates to those calculated by the mixture-based model. As a non-canonical linked model, however, the standard errors did differ slightly from the mixture model. A maximum likelihood estimator used an observed information matrix to produce standard errors. The GLM algorithm produced standard errors, based on the expected information matrix using the difference in standard errors in the negative binomial analyses. The GLM negative binomial algorithm was amended to allow production of standard errors based on the sampled MDR-TB data. The amended GLM-based negative binomial produced identical estimates and standard errors to that of the mixture-based negative binomial analyses. The log-negative binomial data was then imported into an ArcGIS® database, using the spatial analytical tools in SAS/GIS®.

The spatial autocorrelation analysis rendered the results included in Table 2. Results indicated that negligible PSA was detected in the geographic distribution of the clinical and remote-sampled MDR-TB predictor variables. Estimation results from SAS PROC GENMOD for these models appear in Table 3. Positive spatial autocorrelation and NSA spatial filter component pseudo-$R^2$ values are reported. These values did not exactly sum for the complete spatial filter; however, the values were very close to their corresponding totals, suggesting that any induced multicollinearity was quite small.

Rather than switching from a Poisson to a negative binomial probability model, the GLMM was extended to account for latent non-spatial correlation effects, as well as to allow inferences to be drawn for a much wider range of geographic sampling configurations. The GLMM included a random effect, which was specified in this research as a random intercept that was assumed to be normally distributed with a mean of zero, a constant

**Table 5.** A Residual MC minimization of the spatially filtered MDR-TB covariates in the SJL study site.

| Criterion | Positive eigenvectors only | | Positive and negative eigenvectors | |
|---|---|---|---|---|
| | # Eigenvectors | Residual | # Eigenvectors | Residual$\|z_{MC}\|$ |
| Min-Max | 7 | 0 | 7 | 0.4 |

variance, and zero spatial autocorrelation. This varying intercept term compensated for the non-constant mean associated with a negative binomial model GLMM specification. The spatial structuring of random effects was than implemented with a conditional autoregressive model which was generated with a spatial filter.

The GLMM estimation results from SAS PROC NLMIXED appear in Table 4. Notably, an extremely strong linear correlation existed between the negative binomial dispersion parameter estimate reported in Table 4 and the random effects variance estimate reported in Table 3. These spatial autocorrelation components suggested the presence of roughly 14% redundant information in the sampled datasets.

The Residual MC minimization criterion analyses rendered the same set of PSA eigenvectors from the spatial decomposition of the Moran's *I* statistic in a stepwise outcome but in a different order. Spatial filters corresponding to the tabulation of eigenvectors appear in Table 4. No compensatory eigenvectors appeared in the residual MC minimization selection criterion. There were no eigenvectors portraying NSA in the model output (Table 5).

## DISCUSSION

In this research, we demarcated NSA spatial filters in a MDR-TB regression-based model using a Residual MC minimization criterion and a candidate set of eigenvectors from an eigenfunction decomposition algorithm. A Thiessen polygon surface was constructed for partioning the sampled MDR-TB data in ArcGIS using the MC criterion based on the spatial configuration of the health centers at the study site. Spatial filters were constructed from linear combination of eigenvectors calculated from the connectivity matrix representing a surface partitioning for a spatial dataset. In our spatial filtering analyses of the clinical and environmental MDR-TB data, synthetic variates from a set of eigenvectors were extracted with the matrix $(\mathbf{I} - \mathbf{11}^T/n)\ \mathbf{C}\ (\mathbf{I} - \mathbf{11}^T/n)$ which appeared in the numerator of the MC index. This matrix decomposed the Moran's *I* statistic generated using the sampled MDR-TB explanatory covariate coefficients for generating a robust Poisson spatial filtering GLMM. The regression residuals represented spatially independent variable components. Mean, variance and statistical distribution characterizations and descriptions of the georeferenced random variables and their interrelationships were then derived in terms of the eigenfunction spatial filter. The eigenvectors described the full range of all possible mutually orthogonal MDR-TB map patterns based on the spatiotemporal-sampled clinical and environmental covariate coeffcients. The ratio of the areas of the Thiessen polygons to the gridded areas of their corresponding georeferenced health centers were then evaluated for global and local negative dependencies. When the ratios of the actual-to-Thiessen-polygon area ratio were spatially quantified no NSA was detected in the model.

The pioneering nature and the conceptualization of our analysis presented in this research alludes to many themes meriting future spatiotemporal MDR-TB research in the SJL study site. For example, hidden NSA may be detected and qualitatively assessed in a spatiotemporal MDR-TB model which may signify something beyond the more obvious model misspecifications. For example, seasonal MDR-TB model misspecifications may be associated with some anthropogenic population-concentration mechanism at the SJL study site (e.g., rural-to-urban migration) that may require further quantitative monitoring and thereafter inputting as an independent covariate in a robust regression-based inference model. For instance, as people move into areas with little access to piped water as in shantytowns, there may be wider communal use of living quarters at the SJL study site. Additional socio-geographic dependent explanatory covariate coefficients therefore, may add more precision to a predictive spatial autoregressive MDR-TB transmission-oriented model.

Overall, general findings in this research suggest several rules that should help guide a TB researcher in modeling clinical and environment sampled explanatory covariate coefficients in urban environments. Foremost, switching between spatial and non-spatial regression model specifications should yield similar intercept values. Second, non-normal sampled MDR-TB data are best described with non-normal probability models. Third, a Gaussian approximation spatial filter model can be used to quickly explore whether both PSA and NSA components underpin a MDR-TB map; a spatial filter model specification enables a detailed understanding of latent spatial autocorrelation. And, fourth, a Residual MC minimization criterion can be used to determine if hidden NSA furnishes a diagnostic for spatiotemporal MDR-TB model misspecification.

Further, it is important to note that an autocorrelation graph can be employed to determine if a leptokurtic distribution is symmetrical in shape and similar to a normal distribution, while simultaneously quantitating if

the center peak is much higher; that is, if there is a higher frequency of the sampled MDR-TB clinical and environmental covariate coefficients values near the mean. Moran scatterplot and prediction intervals can capture movements from a platykurtic to leptokurtic profile (Anselin, 1995). Leptokurtic distributions in robust spatiotemporal MDR-TB data would then be indicated in the model by higher central peak and larger tails than a normal distribution that persists over time. Theoretically, this output would be counter to the predictions for random walks in homogeneous time series-dependent MDR-TB population database as the central limit theorem (CLT) would predict that the distribution of the distances moved by infected individuals which would approach normality with repeated draws (e.g., seasonal samplings), if the draws are from the same population. In probability theory, the CLT states that, given certain conditions, the mean of a sufficiently large number of independent random variables, each with finite mean and variance, will be approximately normally distributed (Rice, 1995). Okubo (1980) and Skalski and Gilliam (2000) proposed a population heterogeneity hypothesis to explain leptokurtic distributions, drawing from the fact that leptokurtic distributions can be generated as the composite of two or more normal distributions with similar means and contrasting variances. Heterogeneity in infected MDR-TB-related population movement behavior (e.g., from residence to employment sites and primary school locations) as revealed by scatterplots based on leptokurtic distributions could then help derive and quantitate important differences among sexes, age, or social status and disease transmission vulnerability. For example, other clinical explanatory covariate coefficients representing behavioral or psychological variables (e.g., homelessness, alcoholism) and/or more environmental proxy variables associated to MDR-TB transmission (e.g. Euclidean distance measurements to prison) may also reveal differences in MDR-TB transmission-oriented variables within a lagged scatterplot. Robustness testing differences in the variances of the normal distributions of any spatiotemporal-sampled MDR-TB covariates influenced by infected population movement distances, for example, could produce, leptokurtic patterns when plotted together.

Interestingly, the spatial analyses in this research initially produced platykurtic distributions, but the autocorrelation died off exponentially and converged to a Gaussian relatively fast. Population heterogeneity produces leptokurtic distributions of distance moved when a subset of the individuals consistently move longer distance than others (Skalski and Gilliam, 2000; Fraser et al., 2001). When the heterogeneity is in the landscape, not in the individuals, the departures from a Gaussian will eventually be washed out because a particular individual will switch its movement behavior as it encounters patches of different sampled covariates (Betts, 2009).

The speed of convergence is related to how fast the individuals “forget” their previous direction (Fotheringham, 2002). In this research, the distribution of step vectors generated from the regressed MDR-TB covariate coefficients not only affected the rate of convergence but also the way in which convergence was achieved.

A formal treatment of the rate of convergence to a Gaussian in heterogeneous landscapes such as the SJL study site is beyond the scope of this research, but an inspection of the simulation results revealed that the decay of kurtosis with time may be described using our model framework. Thus, the rate of convergence to a Gaussian will also be affected by skewness in spatiotemporal MDR-TB-related movement vectors. In this work, the occurrence of skewed distributions of distance movements at the SJL study site was minimized since there was no external bias in movement direction. The Bayesian Poisson model estimated rates of resistance to each drug by characterizing the endogenous counts, which was thereafter classified by the sampled health center data. For pathogens that must be treated with combinations of antibiotics and acquire resistance through genetic mutation, knowledge of the order in which drug-resistance mutations occur may be important for determining treatment policies. (Reichman et al., 1979) Our Bayesian approach fit branching tree models which revealed that isoniazid and rifampicin were important for MDR-TB treatment in the SJL study site. The standard "short" course treatment for TB-related diseases is isoniazid along with pyridoxal phosphate to obviate peripheral neuropathy caused by isoniazid, rifampicin, pyrazinamide, and ethambutol for two months, then isoniazid and rifampicin alone for a further four months (Iseman 1993).

The residual output from the model alludes to many Bayesian themes for future predictive spatiotemporal MDR-TB research in the SJL study site. For example, once a robust Bayesian probabilistic estimation matrix renders an autoregresssive unbiased estimator it may be kriged using a deterministic interpolator (e.g., inverse distance weighting matrix) which may be employed for time series multivariate prediction of sampled clinical and environmental explanatory covariate coefficients. Since kriging can also be as a form of Bayesian inference (Griffith 2003), a TB analyst could hypothetically begin with a prior distribution over the functions rendered from regressed seasonal-sampled explanatory covariate coefficients. This prior would then be made to take the form of a Gaussian process in the spatiotemporal MDR-TB model. Thus, *N* samples from a function in the model would be normally distributed, whereas, the covariance between any two of the samples would be the covariance function or kernel of the Gaussian process evaluated at a spatial location (for example, georeferenced health center) where the points were sampled, Next, a set of values would then be quantified whereby each value would be associated with the spatial location.

Thereafter, a new sampled clinical value can be predicted at any new spatial location, by combining the Gaussian prior with a Gaussian likelihood function for each of the observed MDR-TB –related Bayesian values. The resulting posterior distribution would also be Gaussian, with a mean and covariance that would then be simply computed from the observed values, their variance, and the kernel matrix derived from the prior.

In conclusion, the spatial analyses of the clinical and environmental covariates sampled in the SJL study site revealed PSA in all models tested; similar log-MDR-TB prevalence rates of the health centers aggregated in geographic space. Our spatial filter model specification enabled an eigenfunction decomposition of the regression residuals, to yield eigenvectors with latent spatial autocorrelation in the sampled data. The orthogonal parameter estimation algorithm allowed each parameter in the non–linear difference equation model to be estimated sequentially and independently of the other explanatory covariates in the model. The spatial filtering analyses transformed all variables containing spatial dependence into covariates free of spatial dependence, by partitioning the original georeferenced attribute variable into two synthetic variates: (1) a spatial filter variate capturing latent spatial dependency, that otherwise would have remained in the response residuals, and (2) a non-spatial variate that was free of spatial dependence. These spatial autocorrelation components suggested the presence of roughly 14% redundant information in the clinical and environmental sampled data. The residual MC minimization criterion analyses found no evidence to suggest that there were negative dependencies present in the model residuals. The algorithm, however, provided unbiased estimates in the presence of correlated noise and provided an indication of which terms to include in the final model. Linear mixed models, autocovariate regression, spatial eigenvector mapping and a residual MC Minimization criterion can be used for qualitatively assessing latent autocorrelation error coefficients in empirical datasets of spatiotemporal-sampled MDR-TB clinical and environmental explanatory covariate coefficients. A lagged-scatterplot can then allow the autocorrelation error coefficients to be displayed .This information can be used for analyzing clinical and environmental sampled MDR-TB data and for implementing control strategies in the SJL study site.

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*Full Length Research Paper*

# Plasmodial infection and haematological parameters in febrile patients in a hospital in Oyo town, South-western Nigeria

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**A cross-sectional study on *Plasmodium* infection was conducted among 158 febrile patients (65 males and 93 females) reporting to Oyo State Hospital, Oyo, South-western Nigeria. Parasitological and haematological examinations of the blood samples were conducted. An overall infection rate of 29.7% was observed with parasite densities ranging from 96 - 64680 asexual parasites/µL blood. The percentages of infected male and female individuals were 27.7 and 31.2%, respectively. The least (12.5%) and the highest prevalence (44.4%) were recorded in age groups <1 and 6 - 15 years respectively. Malaria prevalence and parasitaemia were independent of age and sex (P>0.05). The total leucocytes and lymphocytes decreased with parasites densities, while neutrophils increased with parasitaemia but with insignificant relationships (P>0.05). The neutrophils and lymphocytes in infected and non-infected individuals were (54.0, 55.6%) and (45.9, 43.73%) respectively. The mean packed cell volume (PCV) of the blood in all positive cases in all age groups was lower than in negative individuals. The malaria prevalence in this study was low. Therefore, considerable efforts should further be made to reduce its occurrence below the risk level mostly among the most susceptible groups. Advocacies on the practices of Intermittent Preventive Treatment (IPT) and use of Insecticide Treated Nets (ITNs) should further be promoted.**

**Key words:** *Plasmodium* infection, parasitaemia, prevalence, haematology, Oyo town.

## INTRODUCTION

Malaria causes significant human suffering and impacts on social and economic development. There were 216 million cases of malaria, with 81% of these in the World Health Organization (WHO) African Region. An estimated 3.3 billion people were at risk of malaria in 2010 (WHO, 2011). Malaria remains a major public health problem in Nigeria where it is endemic, especially in rural populations as is the case elsewhere in Africa (Klinkenberg et al., 2005). The World Malaria Report indicated that Nigeria accounts for a quarter of all malaria cases in the 45 malaria endemic countries in Africa, showing clearly the challenge of malaria in Nigeria (WHO, 2008). This maybeduetothelargepopulation;approximately140 million inhabitants (National Bureau of Statistics, 2006) live in areas of stable malaria transmission. Malaria results in 25% infant and 30% childhood mortality (Federal Ministry Health (FMH), 2005a). Also, 11% of maternal deaths are attributed to malaria (FMH, 2000).

More than 90% of the total Nigerian population is at risk of malaria and at least 50% of the population suffers from at least one episode of malaria each year (RBM, 2005; FHM, 2005b). The initiative 'Roll Back Malaria' launched in 1998 in partnership with the United Nations Children's Fund (UNICEF), WHO and many other non-governmental agencies seems not to be producing effective results in some malarial endemic communities of Nigeria as malaria problem is still on the increase. Many studies have reported high prevalence rates of malaria in pregnancy in different parts of Nigeria, ranging from 19.7 to 72.0% (Okwa, 2003; Adefioye et al., 2007; Kagu et al., 2007). With such reported high prevalence, there is a

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**Table 1.** Age and sex prevalence of malaria in febrile patients reporting to Oyo State hospital

| Age (years) | Male | | Female | | Total | |
|---|---|---|---|---|---|---|
| | No. examined | No. infected (Prevalence) | No. examined | No. infected (Prevalence) | No. examined | No. infected (Prevalence) |
| <1 | 11 | 0 (0) | 5 | 2 (40) | 16 | 2 (12.5) |
| 1-5 | 18 | 8 (44.4) | 15 | 3 (20) | 33 | 11 (33.3) |
| 6-15 | 14 | 6 (42.9) | 13 | 6 (46.2) | 27 | 12 (44.4) |
| 16> | 22 | 4 (18.2) | 60 | 18 (30) | 82 | 22 (26.8) |
| Total | 65 | 18 (27.7) | 93 | 29 (31.2) | 158 | 47 (29.7) |

$\chi^2 = 5.72$; $P>0.05$.

need to determine the extent of infection by *Plasmodium falciparum* in endemic communities of Nigeria as this will help in the proper management of the disease.

Haematological changes are some of the most common complications in malaria and they play a major role in malaria pathology. These changes involve the major cell lines such as red blood cells, leucocytes and thrombocytes (Maina et al., 2010). Haematological abnormalities such as anaemia, thrombocytopenia, and Leukocytosis or leucopenia have been observed in patients with malaria (Ladhani et al., 2002, Maina et al., 2010). The extent of these alterations varies with the level of malaria endemicity, background haemoglobinopathy, nutritional status, demographic factors, and malaria immunity (Price et al., 2001). Severe anaemia is the predominant severe malaria syndrome peaking in the first two years of life and is attributed to *P. falciparum* ((Waitumbi et al., 2000). In malaria-infected patients, especially non-immunes children, prompt and accurate diagnosis is key to effective disease management for a favorable outcome (Miana et al., 2010).

This study reports the prevalence of malaria parasitaemia caused by *P. falciparum* and also determines the changes in the haematological parameters of the febrile patients in Oyo town in South-western Nigeria.

## MATERIALS AND METHODS

### Study area

The study was carried out in Oyo, an urban town in Oyo State, South-western Nigeria. It lies in the tropical rainforest belt, and according to the 1991 census had an estimated population of 3,452,720. Oyo town is made up of three Local Government Areas namely; Oyo West, Oyo East and Atiba. The native language in Oyo is Yoruba.

### Study design

Ethical clearance to conduct the study was obtained from the University of Ibadan/University College Hospital Ethical Approval Committee. Prior to the commencement of the study, permission was sought from the management of Oyo State Hospital, Oyo. Subjects included patients of all ages reporting to the hospital and directed to the hospital laboratory for blood screening for malaria parasites. All individuals that volunteered to participate were recruited for the study. Participants' consents to participate in the study were also sought and were duly informed of the significance of the study. The study was carried out between January and February, 2007, towards the end of the dry season. Parasitological and haematological examinations were done in the Oyo State Hospital, Oyo.

### Preparation and examination of blood films

Blood samples were obtained from patients by trained laboratory staff on duty. Thick and thin blood films were made by spreading a drop of blood on a clean, grease-free, labelled slide and then allowed to dry. The dried blood films were then stained with 10% Giemsa stain solution and washed after 10 min using clean water. The stained films were allowed to dry and on addition of a drop of immersion oil, each slide was examined under ×100 objective lens for malaria parasites. The densities of positive slides were estimated by the methods described by Cheesbrough (1999).

### Haematological examination

The packed cell volume (PCV) was determined by haematocrit centrifugation technique (Jain, 1986). Total white blood cell counts and differential white blood cell counts were carried out using standard haematological techniques (Cheesborough, 2005).

### Statistical analyses

Data was entered into an Excel spreadsheet, checked for entry errors and transferred into SPSS for Windows (version 17.0, SPSS Inc, Chicago, USA) for analyses. Students' t-test was used to determine significant differences in the density of infection by *P. falciparum*. Differences in proportions were tested by Chi-square tests. Contingency Chi-square ($\chi^2$) analysis was used to determine the association between prevalence and intensity of infection across age groups. Pearson's correlation coefficient was used to test the relationships between infection and blood parameters.

## RESULTS

A total of 158 patients were screened for malaria parasites in the Oyo State Hospital laboratory. Of these, 47(29.7%) were positive to *P. falciparum*. The prevalence of infection was not significantly associated with age and sex (Table 1). The geometric mean of parasite density

**Table 2.** Distribution of age-related density of parasite in febrile patients reporting to Oyo State hospital.

| Age (years) | Parasite density (asexual parasites/µL) | | | |
|---|---|---|---|---|
| | 1-400 | 401 - 6400 | >6400 | Total (%) |
| <1 | 1 (2.1) | 1 (2.1) | - | 2 (4.3) |
| 1-5 | 5 (10.6) | 4 (8.5) | 2 (4.3) | 11 (23.4) |
| 6-15 | 1 (2.1) | 7 (14.9) | 4 (8.5) | 12 (25.5) |
| 16> | 11 (23.4) | 9 (19.1) | 2 (4.3) | 22 (46.8) |
| Total | 18 (38.3) | 21 (44.7) | 8 (17.0) | 47 (100) |

$\chi^2$ =7.63, P>0.05.

**Table 3.** Mean white blood cells (WBCs) counts, in relation to malaria infection.

| Blood parameter | Leucocytes ± SE (cell/mm$^3$of Blood) | Neutrophils ± SE (cell/mm$^3$of Blood) | Lymphocytes ± SE (cell/mm$^3$of Blood) |
|---|---|---|---|
| Infected | 9263.96 ± 6171.89 | 54.02 ± 19.85 | 45.87 ± 19.79 |
| Non-infected | 9804.26 ± 8113.14 | 55.60 ± 21.86 | 43.72 ± 21.64 |

*The differences in the mean values of the infected and non-infected subjects were not significant (P>0.05).

**Table 4.** Mean (± SE) PCV in relation to age and malaria infection status.

| Age (years) | <1 | 1-5 | 6-15 | 16> |
|---|---|---|---|---|
| Infected | 25.50 ± 6.36$^a$ | 24.00 ± 6.99$^a$ | 29.33 ± 5.69$^a$ | 35.68 ± 4.90$^a$ |
| Non-infected | 30.43 ± 5.03$^b$ | 32.15 ± 5.27$^b$ | 33.00 ± 8.46$^a$ | 35.82 ± 8.04$^a$ |

*The differences in the mean values of PCV of infected and non-infected subject was not significant (P>0.05), but was significant in age groups <1 and 1 - 5 years.

was 1170 parasites/µL of blood. Mean parasites intensities were 7.3 ± 5.4, 808 ± 542.4, 689 ± 322.1 and 667 ± 364.7 asexual parasites/µL of blood in age groups < 1, 1-5, 6-15 and 16> years, respectively. The prevalence and intensity of infection were not age-dependent (P>0.05) (Table 2).

Moreover, there were no significant variations in the mean values of the total leucocytes counts, neutrophils and lymphocytes counts in infected and non-infected individuals (Table 3). However, the mean PCV values were significantly higher in non infected individuals (32.15±5.27) than in infected individuals (24.00 ± 6.99) in age group 1 - 5 years (Table 4). Total leucocytes counts and lymphocytes decreased with parasites density (r = -0.092, -0.07) while neutrophils increased with parasite density (r =0.012), but these relationships were not significant (P>0.05).

## DISCUSSION

Prevalence of malaria in urban environments is generally lower than in the rural communities. The low levels of malaria incidence in the urban settlements could be as a result of relatively good effective alert systems on malarial control. Anopheles mosquitoes may also be less abundant due to the urban pollution. However, high disease impact may result due to lack of repeated infections with multiple strains of malaria parasites in urban settings (Klinkenberg et al., 2005). Tolerance to malaria parasitaemia does occur naturally, but only in response to repeated infection with multiple strains of malaria, especially among adults in areas of moderate or intense transmission conditions (Färnert et al., 2009; WHO, 2010).

The overall prevalence of malaria in this study was low (29.7%). The value was higher than 17 and 7.7% overall prevalence reported by Anumudu et al. (2006) and Oyibo et al. (2009), among the University of Ibadan campus students and pregnant women in Lagos, South-western Nigeria, respectively. On the other hand, the overall prevalence of malaria reported in this study is substantially lower than previous estimates from other studies in peri-urban areas of Nigeria and other parts of West Africa (Ojo and Mafiana, 2005; Umeaneato and Ekejindu, 2006; Maina et al., 2010). This rather low prevalence could be attributed to the dry season during which the study was carried out. High rainfall and humidity increases mosquito

longevity and give room to the collection of clear, still, sun exposed waters, all of which enhance malaria transmission, serving as good vector breeding sites (Breman, 2001).

Moreover, in this study, it was found that female individuals have a higher risk of being infected with malaria compared to the male participants. This is in accordance with other reports (Ibekwe et al., 2009; Okonko et al., 2009; 2010). However, the reverse trend has been reported in some other studies (Askling et al., 2005; WHS, 2006; Abdullahi et al., 2009). Attitudes of women such as getting up before dawn to perform household chores may expose them more to mosquitoes and consequently to malaria infection than their male counterparts (Vlassoff and Manderson, 1998). In addition, pregnant women are more attracted to the bites of *Anopheles gambiae* complex, the predominant African malaria-carrying mosquito, than did their non-pregnant counterparts and other population groups due to some physiological and behavioral changes that occur during pregnancy (Lindsay et al., 2000). Generally, the study showed gradual increase in prevalence with age with the highest prevalence recorded in age group 6 - 15 years. However, our study contradicted other findings that showed higher prevalence among children (<15 years of age) (Umar and Hassan, 2002; WHO, 2005). The 44.4% prevalence in the age group 6 - 15 years reported in this study corroborates with the WHO (2004) and UNAIDS/WHO (2009) 42.7% prevalence. This age group therefore constitutes the group with significantly high risk of malaria. The low malaria prevalence (26.8%) among the adults (15> years) could be due to the acquisition of immunity after continued exposure from multiple malaria infections over time (Plebanski and Hill, 2000).

The haematological abnormalities previously reported included changes in haemoglobin, leukocyte count, platelet abnormalities resulting in defective thromboplastin, and disseminated intravascular coagulation (DIC) (Richards et al., 1998). In this study, although leukocytosis was frequently seen in the malaria-infected subjects, no significant difference in WBC was found between the two groups. In contrast, other studies have demonstrated leucopenia (Erhart et al., 2004; Lathia and Joshi, 2004) or leukocytosis (Ladhani et al., 2002). These findings are comparable with those of other studies (Bashawri et al., 2002; Maina et al., 2010) that reported no significant difference in WBC between the malaria infected and non-infected groups. Meanwhile, our results on lack of association between malaria and neutrophil count deviated from previous studies that showed significantly higher neutrophil count in children with malaria compared to the non-malaria infected children (Bashawri et al., 2002; Ladhan et al., 2002; Maina et al., 2010). Higher lymphocyte count reported among malaria infected subjects in our study was also in contrast to other studies that showed that decrease lymphocyte count was associated with malarial parasites infection (Richard et al., 1998; Erhart et al., 2004). The high level of lymphocytes could be due to its distribution into the peripheral blood during malarial infection.

Anaemia is one of the most common complications in malaria, especially in younger children and pregnant women in high transmission areas (Menendez et al., 2000). It is thought to result from a combination of haemolytic mechanisms and accelerated removal of both parasitized and non-parasitized red blood cells, depressed and ineffective erythropoiesis (Weatherall et al., 2002). Generally, the present study showed higher susceptibility of children in the age group 0 - 15 years to anaemic condition than the adult population. The significantly lower PCV values recorded among the *P. falciparum* parasitized younger children (0 - 5 years) further explain the implication of malaria in causing anaemia in the group. The low PCV values recorded among few non-parasitized subjects may in part reflect poor nutritional status, background haemoglobinopathy, intestinal worm infestation and previous and/or repeated malaria infections in this area (Maina et al., 2010).

In conclusion, malaria prevalence in the study area was low compared to some other investigations. Although being an urban setting, effective system could be responsible for the low level. However, this cannot be fully justified until similar study is carried out in the study area during the rainy season. This will enable us to evaluate the influence of seasons in the dynamics of the disease.

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*Full Length Research Paper*

# Prevalence of cockroaches *(Periplanata americana)* in households in Calabar: Public health implications

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**The study was carried out in Anantigha area of Calabar, Nigeria and involved the trapping and examination of cockroaches from toilets, kitchens, living rooms and bedrooms of houses to determine the parasites in and on the cockroaches and also to assess the possible role of the cockroaches in the dissemination of medically important parasites. A total of 322 cockroaches were trapped from the different sites within the households and all identified as *Periplananta americana* species. Out of the 322 cockroaches examined, 58.6% were infected with one or several species of gastrointestinal parasites. Parasites isolated and identified include *Balantidium coli* (8.8%), Hookworms (9.6%), *Entameba coli* (10.4%), *Enterobius vermicularis* (12. 9%), *Entameba histolytica* (13.7%), *Trichuris trichuira* (16.9%) and *Ascaris lumbricoides* (24.4%). Cockroaches collected from the toilets had the highest parasite load of 4 to 54 parasites/ml followed by those from the kitchen with 1 to 24 parasites/ml, and those from the living room 1 to 12 parasites/ml while 1 to 10 parasites/ml was observed from cockroaches from the bedroom. No cestodes were encountered in this study. More parasites were recovered from the external than in the gastro-intestinal tract with prevalence rates of 65.3 and 34. 6%, respectively. The presence of gastro-intestinal parasites was significant since these parasites can easily be transferred by the cockroaches to humans. This study has shown that cockroaches represent an important reservoir of important parasites which can cause disease in man. It also highlights the potential of cockroaches as mechanical transmitters of parasite ova and cysts which they pick up from faeces and transfer to food by crawling. There is need to control cockroaches indoors and outside.**

**Key words:** Cockroaches, parasites, mechanical transmission, Calabar, Nigeria.

## INTRODUCTION

Cockroaches are found all over the world with about 3500 known species. They are among the notorious pests that are found in households, supermarkets, public places, and refuse dumps. In addition to their repulsive and annoying characteristics, they eat and contaminate food and leave a persistent offensive odour in infested places (Revault et al., 1993; Pai et al., 2004) and Lemons et al. (2006). Cockroaches are nocturnal and omnivorous and these characteristics make them ideal carriers of pathogens. According to Tatfeng et al. (2005), cockroaches are known to carry bacteria, protozoa, helminthes fungi and viruses, however, their role or direct transmission of these infectious agents has not been really established. According to Pai et al. (2004) and Salehzadeh et al. (2007), parasites have been found on the external parts of cockroaches. Also, Kim and Zong (1974) Thyseen et al. (2004) and Chan et al. (2004) have also shown that cockroaches are carriers of medically important organisms.

Cockroaches are something that many people are worried about when they see them in their homes. This is

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because the presence of cockroaches indicates unsanitary conditions. According to Graczyk et al. (2005) cockroaches are known to carry organisms that cause diseases like dysentery, typhoid and polio as well as gastroenteritis because they live on anything from fermenting products, rotting food, faeces, fresh food and then move from one location to another with ease. Their filthy breeding habits, feeding mechanisms and indiscriminate travel between filth and food make them efficient vectors of human enteric parasites Cockroaches can cause potentially serious health problems, provoke allergic reactions and as have been suggested possible vectors by Thyseen et al. (2004), Getachew et al. (2007), Tatfeng et al. (2005) and Fakoorziba et al. (2010). Cockroaches not only contaminate food with their droppings but can also cause food poisoning (Pai et al., 2004). According to Tatfeng et al. (2005), some people are allergic to antigens and faeces of cockroaches which may result in asthmatic – related health problems. Even though no one exposes himself to their faces on purpose, it can be inhaled through particles of dust in the air. Food can also be contaminated with the faeces of the cockroaches, dead cockroaches and salivary gland excretions. So, the presence of even a cockroach is not to be overlooked as they can multiply and spread very fast. This is because they secrete a pheromone in their faces which attracts other cockroaches, with a quick buildup in unsanitary conditions. Cockroaches live in groups and are attracted to humidity, warmth and darkness and are common in toilets, bathrooms, kitchens and dining and bedrooms. The mere sight of cockroaches cause considerable emotional distress due to the strong repulsive odour they emit. Their presence in households is of epidemiological significance due to their nocturnal and filthy habits (Cruden and Markovetz, 1987). Their nocturnal and filthy habits make them ideal carriers of parasites.

This study assessed the prevalence of parasites of cockroaches and the potential of the cockroaches in diseases transmission in Calabar. Parasites were isolated from the external and gastro-intestinal tract of the gastro-intestinal tract of cockroaches.

## MATERIALS AND METHODS

### Study area

The study was carried out between January and June, 2011 in Anantigha area of Calabar. Anantigha is a peri-urban community where sanitary conditions are below standard. There is no pipe-borne water supply and the people rely on wells and commercial bore holes for their water needs. The area was chosen because of the low sanitary conditions and presence of refuse heaps which attracted flies and cockroaches. Some households still used pit latrines for defecation since there was no adequate water supply for water closet toilets. Some houses with water closets lacked water for proper use and the toilets were usually in a poor sanitary condition. Temperature in Calabar ranges between 28 and 32°C and mean annual rainfall is 1830 mm. There are two distinct seasons; the rainy season (April-September) and the dry season (October-March).

### Sample collection

Three hundred and twenty two (322) adult cockroaches were trapped from different parts of the 65 households selected randomly from the community for the period of the survey. Fifteen houses were separate bungalows having single family units while 50 houses were buildings with many families who shared facilities, kitchens, bathrooms and toilets. Only whole and live cockroaches were used for the study. The cockroaches were caught at night on sticky traps placed against vertical surfaces corners and floors of the kitchen, toilets, bathrooms, bedrooms and living rooms from households in different parts of the community. Each cockroach after collection was put in a sterile universal container and transported within an hour to the Biology Laboratory of Cross River University of Technology, Calabar, for further examination. The cockroaches were killed individually by using chloroform-soaked cotton wool and examined under the dissecting microscope for identification using standard taxonomical keys.

### Isolation of parasites from the external surface of the cockroaches

After identification, 2 ml of normal saline was added to the universal container with the cockroach and shaken for 2 min to detach the parasites on the surface of the cockroach. 1 ml of the washing fluid was then transferred to a centrifuge tube and centrifuged at 2000 rpm for 5 min. The supernatant was discarded and the deposits stained with 1% Lugol's iodine and examined using light microscope ×40 objective lens as described by Salehzadehah et al. (2007). Parasites were identified using taxonomical keys and counted.

### Isolation of parasites from the gastro-intestinal tract of the cockroaches

After the external examination, the cockroaches were separately placed in 70% ethanol for five minutes (to remove parasites from the external surfaces) and then washed in sterile saline to remove the alcohol from the body of the cockroaches. They were allowed to dry at room temperature. The cockroach was then fixed on a dissecting Petri-dish, the head severed first, followed by the legs, then the abdomen was opened using fine pointed forceps and discarded. The gut and other abdominal organs were removed using fine needles. The intestine was then examined over a black background for detection of parasites. 2 ml normal saline was added and the intestine macerated. 1 ml of the macerate was centrifuged at 2000 rpm for 5 min and the deposits stained with 1% Lugol's iodine before examination. Ova and cysts of parasites present were identified using taxonomical keys and counted using ×40 objective lens of the light microscope.

## RESULTS

A total of 322 cockroaches were collected during the period of survey from the 65 households examined and all were identified as *Periplenata americana*. The study revealed that these cockroaches trapped from different places in the houses (toilets, kitchen, living rooms and bedrooms) harboured various microorganisms with an

**Table 1.** Number of infected cockroaches trapped in various sites in the 65 households in Calabar.

| Location | No. of cockroaches examined | No. of cockroaches with parasites infected | Percentage infection rate | Parasites/ml mean range |
|---|---|---|---|---|
| Toilets and latrines | 160 | 102 | 63.7 | 4 – 65 |
| Kitchens | 112 | 64 | 57.1 | 1 – 24 |
| Living rooms | 28 | 13 | 46.4 | 1 – 12 |
| Bedrooms | 22 | 10 | 45.4 | 1 – 8 |
| Total | 322 | 189 | 58.6 | |

**Table 2.** Types of parasites and percentage infection rate presence of parasites on cockroaches examined.

| Type of infection | No. of cockroaches infected | No. of parasites isolated | Percentage infection rate |
|---|---|---|---|
| Helminthes | 151 | 166 | 79.8 |
| Protozoa | 38 | 82 | 20.1 |
| Total | 189 | 248 | |

**Table 3.** Parasites infection present on external and gastro-intestinal tract of cockroaches in Calabar.

| Site examined | No. of cockroaches infected | No. of parasites isolated | Percentage infection rate |
|---|---|---|---|
| External surface | 189 | 162 | 65.3 |
| Internal surface gastro-intestinal tract | 189 | 86 | 34.6% |
| Total | 189 | 248 | |

infection rate of 58.6%. A total of 248 organisms of medical importance were identified and comprised, cysts of *Balantidium coli* (8.8%) Hookworms (9.6%), *Entameba coli* cysts (10.4%), *Enterobius vermicularis* (12.9%), *Entameba histolytica* cyst (13.7%), *Trichuris trichuira* (16.9%), *Ascaris lumbricoides* (27.4%), collected from the external and internal surfaces gastro-intestinal tract of the cockroaches collected. There were mixed infections in some cockroaches as 30.6% of the cockroaches examined harboured all the parasites identified, 16.9% had four parasites each, 14.8%, two parasites each while 14.2% had five parasites each and 11.6% had one parasite while 1.5% had three parasites each. No cockroach had five parasites. Cockroaches collected from the toilets and latrine had the highest infection rate of 63.7% followed by cockroaches collected from the kitchen with 57.1%, those from the living room 46.4% while those from the bedroom had 45.4% as shown in Table 1. shows percentage of cockroaches that had parasites. Those with the highest percentage of infection rate were cockroaches collected from the toilets.

Table 2 shows that more helminthes and protozoa (79.8% and 20.1%) were isolated from the cockroaches More parasites, 65.3% of total parasites obtained were isolated from the external surface than the gastro-intestinal tract that had 34.6% (Table 3).

Figure 1 shows that *A. lumbricoides* was the largest in number most common parasite while the least common

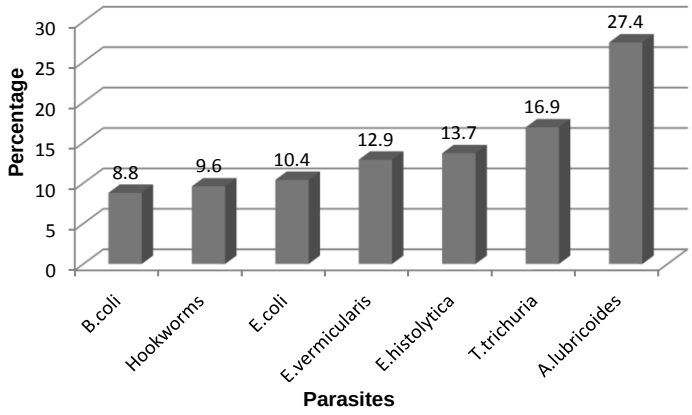


**Figure 1.** Percentage of the various parasites isolated from the cockroaches.

was *B. coli*

## DISCUSSION

Speculations have always been made on the involvement of cockroaches as possible vectors of diseases in our communities. However, very few studies are available on this issue. Findings from this study indicated that cock-roaches may play an important role in the trans-mission of some parasites especially those isolated and identified.

Parasite infection rate of 58.6% observed on the cockroaches observed in this study is quite sig-nificant. This is comparable with results by Chamavit *et al.* (2011) but lower that Al-Mayali and Al-yaqoobi (2010) who reported infection rates of 54.1 and 83.33% respec-tively. This high prevalence recorded in Anantigha area of Calabar may be due to unsanitary conditions coupled with low socio economic status of the people. Organisms identified in this study are all known parasites which pro-duce disease in humans and is similar to Tachbele et al. (2006). All the collected cockroaches were identified as *P. americana.* Results in this study are similar to results by Pai et al. (2003) and Chan et al. (2004) who stated that significant since cockroaches are known as carriers of infectious agents and significantly contribute to the spread of parasitic infections, this is similar to the report by Chan et al. (2004). Poor faecal and garbage disposal systems observed in this area, contribute to the proliferation of cockroaches and parasitic contamination of the cockroaches with resultant possible transmission of these parasites to human food when by the cockroaches crawl about. It is important to note that the cockroaches collected from the toilets had more parasites because they were easily exposed to and contaminated by faecal matter. As a result of their high mobility of the cockroaches, they easily deposit parasites carried on their bodies or within them on food and other parts of the house when they move about. Cockroaches from houses with pit latrines had higher mean parasite count when compared to those trapped from houses with water system toilets (with 65 and 52 parasites/ml) respectively. This variation could be explained by the fact that pit latrines are more accessible to the cockroaches and these also provide more favourable hide-outs during the day while the cockroaches move during the day into the house at night in search of food.

Our findings show that there are many parasites of public health significance carried and harboured by cockroaches in Calabar. Unfortunately, the people did not consider presence of cockroaches and parasitic infections as a serious problem, even though they did not like the sight of cockroaches.

The isolation of these parasites from the cockroaches indicated that these pests could pose health problems to humans who may overlook their potential role in the spread of these parasites.

Although it is difficult to prove the direct involvement of cockroaches in the direct transmission of pathogenic agents, it is important to note that since they carry patho-genic organisms that are of public health and medical importance inside and on their bodies, they can be incriminated in the mechanical transmission; these organisms then they move about from faeces to food and vice versa.

## Conclusion

Cockroaches constitute an important reservoir for pathogens; therefore the control of cockroaches is important since this will reduce the spread of parasitic diseases transmitted by cockroaches in the community. Cockroaches represent a risk for humans even though their involvement in biological transmission of diseases is still difficult to demonstrate and be determined. Control and management of cockroach infestations in Calabar and elsewhere should be conducted to reduce their spread. This should involve daily emptying of garbage and proper disposal along with and elimination of the cockroach habitats and the cockroaches within the home using insecticides.

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*Full Length Research Paper*

# Perceived needs for school mental health among stakeholders in districts of South-west Nigeria

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**Child and adolescent mental health problems could cause significant distress, and may limit the chance of a student to fully utilize his or her potentials. School mental health services (SMHS) are standard practices in many parts of the world and serves as a useful preventive intervention against child/adolescent psychiatric disorders. The study is aimed at determining teachers, students and parents beliefs about the need for school mental health services in a sample of secondary schools in south west Nigeria. A cross sectional descriptive study was conducted within two educational district areas of south west Nigeria. Six schools were included in the survey. A total of 697 students, 51 teachers and 376 parents were recruited to the survey, after written consent was obtained from teachers and parents. Information was gathered using anonymously filled socio-demographic questionnaire and pre-designed an attitude/beliefs questionnaire that explored for school mental knowledge, needs and services. A few (11.1%) of the respondents had some school mental health service in their school; 75.8% said it did not exist, while 13.1% were not sure. 58.6% had school drug abuse free clubs. 20.7% knew there was a school counsellor; 67.4% said none existed and 11.9% were unsure. Aggressive behaviour (52.7%) and unexplained absenteeism (35.0%) were the commonest mental health challenges identified by the stake holders in their schools that will benefit from SMHS. There is a need for school mental health services in this study location.**

**Key words:** School mental health, stakeholders, services, Nigeria.

## INTRODUCTION

Researchers have consistently seen schools as a neutral ground where children mental health needs can be detected and addressed (Adelman anf Taylor, 2000; Bruns et al., 2004; Sugai et al., 2000; Zins et al., 2004). Some advocates for children mental health care and school based health centers (Stroul and Feidman, 1996; Advocates for Youths, 1998) have underscored the useful impact of having integrated services in the school setting to aid in recognizing, assessing and treating children's mental health problems.

Prevalence rates of psychiatric disorders have been found to range from 12 to 29% among children visiting primary care facilities in various countries (Giel and Harding, `1976). Only 10 to 22% of these cases are recognized by primary health workers, so majority of children do not receive appropriate services. However many more have problems that can be considered "sub threshold" and will also benefit from interventions, but only if they are detected. The potentially undetected sub threshold cases can often be attended to or picked through the school mental health system. Children and adolescents seldom decide for themselves when to seek out health services for physical or emotional problems and though parents, teachers and other care givers can easily recognize many physical conditions, the emotional disorders are often not so readily apparent. There is an increasing call worldwide on schools to include school mental health promotion in school curricula and policies (Weist and Murray, 2008). There are a wide range of issues arising in health and social sector that further buttress the need for a more deliberate inclusion of such services from the school system; these issues range from drug use and abuse, HIV and risky sexual behaviour, teenage pregnancy and youth suicide prevention, self harm and more recently, cyber bullying. Currently many school based services provide the practice of mental

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health services in and for schools. There is however a growing expansion of the concept of school mental health promotion to achieve a more balanced approach with a positive and enhancing focus.

School mental health promotion can be defined as the act of providing a full continuum of mental health promotion programs and services in schools, including enhancing environments, broadly training and promoting social and emotional learning and life skills, preventing emotional and behavioural problem, identifying and intervening in these problems early on, and providing intervention for established problems (Weist and Murray, 2008). School mental health promotion programs should be available to all students, including those in general and special education, in diverse educational settings and should reflect a shared agenda – with families and young people, school and community partners actively involved in building, continuously improving, and expanding them. However, the attitudes and perception of need as felt by relevant stakeholders can determine the use of these services. Teachers in particular, have the opportunity to detect majority of problems in school as students spent several hours in their custody. Some researchers have found that in most places the attitudes of teachers towards Child and Adolescent Mental Health Services (CAMHS) has been good, as displayed by appropriate referrals when necessary (Ford and Nikapota, 2000), and others have found that teachers knowledge about mental health issues are limited and they often do not feel confident about their ability to manage mental health problems in their class rooms (Walter et al., 2006). Child psychiatrists are continuously encouraged to collaborate with teachers to promote mental health and manage children with behavioural and psychological problems (Tamsin and Nikapota, 2000).

In Nigeria, Child and adolescent psychiatry is an evolving subspecialty and though many schools offer school health services, school mental health content are rudimentary or nonexistent. Some researchers have made effort to investigate the need for the provision of these services and the perception regarding mental health care provision in the school setting (Dogra et al 2012; Bella et al., 2009; Omigbodun et al., 2009). In certain parts of Nigeria, teachers have expressed negative attitudes towards mentally ill persons but are still able to describe kinds of mental illnesses in children (Ibeziako et al., 2008). Parents and students are important stakeholders in the development of school mental health services, their perceptions of need or illness will also determine the use of services.

Lagos as the economic center of Nigeria is the State with the largest population in the country. Though the state provides school health services, these services are majorly focused on health screening and care of school children in the areas of; adequate nutrition, de-worming, ear nose and throat conditions and other physical health conditions. Mental health is still not appropriately represented in any of these interventions to schools. Though limited local studies have examined how relevant stakeholders like students/parents/teachers and educational authorities view such school mental health services in some other parts of Nigeria (Ibeziako et al., 2008), there is still a need for more useful data that provides further description of some stakeholders current experiences, needs and beliefs about such services. This study aimed to determine the perspectives held by key stakeholders, that is, teachers, parents and students. These findings may be useful towards providing client centered and culturally sensitive school mental health care in Nigeria.

## METHODS

### Study design and setting

The study was cross-sectional and descriptive in nature. It was carried out in Lagos State, which is one of the 36 states in Nigeria. Lagos State is broadly described as Lagos Mainland and Lagos Island regions. The study population came from the Lagos Mainland area. These schools are run as Junior Secondary comprising of Basic 7 to 9 (also called JSS1 –JSS3), these are the first three classes in Secondary School and senior secondary which are the 3 last classes before completing secondary schools (SS1 – SS3).

### *Instruments*

Data collection was by questionnaires. The main questionnaire was self administered comprising of of 12 questions enquiring about the socio demographic details of the respondent, the questions were designed with details specifically to suit each cadre of stakeholders. Similar constructs were assessed across each group but the language was adapted to suit the peculiarity of that group. There were additional questions that assessed:

Opinions on the need for schools mental health services, types of disorders that require such services, the inclusion of mental health content in the curriculum and further details about their opinions on; where, when and who should provide such services. Knowledge about some mental health related disorders that were enquired about included; Depression/extreme sadness, unexplained fear, bullying, suicide, unexplained absenteeism (which may be suggestive of a conduct problem or early antisocial traits).

The stakeholders were asked similar questions in all aspects but language was suited to meet the needs of each group.

A pilot study to pretest the questionnaires was carried out among 10 students, 10 parents and 4 teachers from two schools that were not entered in the study. Following the pilot study, necessary modifications were carried out on some of the questions to make them easier to understand by the respondents.

### *Participants and procedure*

There are six educational district areas in the state and the participants were drawn from the mainland and Surulere educational districts, being closely adjoined to one another and each having a total of 17 and 58 schools, respectively. The final six schools in this study were chosen randomly from a table of random numbers with 2 and 4 schools chosen from the aforementioned education districts respectively. In each school, 12 teachers were chosen (6 from junior and 6 senior secondary). Teachers were

**Table 1.** All respondents and school mental health.

| Characteristic | Frequency (n) | % |
|---|---|---|
| **Respondent** | | |
| Student | 697 | 62 |
| Teacher | 51 | 4.5 |
| Parent | 376 | 33.5 |
| **Gender** | | |
| Male | 734 | 65.3 |
| Female | 390 | 34.7 |
| **Ever heard of School Mental Health** | | |
| Yes | 295 | 26.2 |
| No | 615 | 54.7 |
| Don't know | 214 | 19 |
| **Do you know if your school has SMHS** | | |
| Yes | 125 | 11.1 |
| No | 852 | 75.8 |
| Not sure | 147 | 13.1 |
| **Do you know if school has drug abuse free clubs or groups?** | | |
| Yes | 659 | 58.6 |
| No | 378 | 33.7 |
| Don't know | 87 | 7.7 |
| **Is there a school counsellor** | | |
| Yes | 233 | 20.7 |
| No | 757 | 67.4 |
| Don't know | 134 | 11.9 |

randomly chosen to participate in each school using table of random numbers. Each teacher along with the researcher selected 6 parents each and 10 students from their classes who were also chosen to partake in the survey; these were selected using table of random numbers. The selected students were called to the school hall and completed the questions after being reassured about anonymity and confidentiality. Parents had forms sent to them for return to the school within a week.

The final study sample attained was 1124 made up of 51 teachers, 376 parents and 697 students. The response rate among the students was 96.0%, parents 87.0% and teachers 70.8%.

#### Ethical considerations

Approval for the study was obtained from the Educational district authorities and the Principals of the schools. Teachers and parents who participated in the selected schools also were given a detailed information document on the purpose of the study and informed consent was obtained before enrollment as participants. Selected students also provided written consent from their parents before participating.

#### Data analyses

Data analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 17. Presentation of data was by using simple frequency distribution table, with absolute numbers and percentages to the nearest tenth.

## RESULTS

### Respondents and school mental health

A total of 1124 respondents were included in the study, of these 697 (62.0%) were students, 51 (4.5%) were teachers and 376 (33.5%) were parents. Of these 734 (65.3%) were male. Only 295 (26.2% of them had ever heard of school mental health services before, while 615 (54.7%) had never heard of it, 214 (19.0%) were unsure. 125 (11.1%) knew and their school had mental health services and 75.8% did not know. Though there were drug free clubs in 58.6%, only 20.7% claimed they had a school counsellor (Table 1).

### Stakeholders characteristics and prior knowledge of school mental health service (SMHS)

Parents were 376 in number; most were aged between 41 and 80 years (59.4%) while some were below age 40 (40.6%), and others over 61.6% had above secondary school level of education. The teachers were 51 in number; 51% were male and 46 (90.2%) had appropriate quailfication to teach. 52.9% taught the junior secondary school students while 47.1% taught the senior secondary school students. Only 5(9.8%) claimed to address mental health in curricula they taught. 36(70.6%) had over 10 years of working experience (Table 2).

The students were 697 in number, 74.3% were aged 13 to 15 years and 25.7% were aged between 16 to 19 years; 522 (74.9%) were male and 60.5% of them were from the senior secondary classes while 39.5% were from the junior secondary school. 33.4% of the students believed they learn about mental health issues while 66.6% say they do not.

### Reported mental health problems

Mental health problems observed by the different respondent groups include Depression (24.6%), aggression (52.7%), Bullying (35.2%), unexplained fear (32.6%), unexplained absenteeism (35.0%); substance abuse and suicide attempts were both the least reported with 9.2 and 11.9%, respectively. Aggression and absenteeism appeared to be the most common mental health problems noticed by the stakeholders in these schools (Table 3).

### Understanding and experience around SMHS

Comparing the 3 groups of respondents and their prior

**Table 2.** Stakeholder characteristics and prior SMHS knowledge.

| Characteristic | n | % |
|---|---|---|
| **A. Parents** | | |
| Age group | | |
| 20-40 | 151 | 40.6 |
| 41-80 | 221 | 59.4 |
| Gender | | |
| Male | 156 | 46.7 |
| Female | 176 | 52.7 |
| Level of education | | |
| Primary | 39 | 10.5 |
| Secondary | 229 | 61.6 |
| Polytechnic | 29 | 7.8 |
| University | 72 | 19.4 |
| Others | 3 | 0.8 |
| **B. Teachers** | | |
| Gender | | |
| Male | 26 | 51.0 |
| Female | 25 | 49.9 |
| Teaching qualification | | |
| Yes | 46 | 90.2 |
| No | 5 | 9.8 |
| Class taught | | |
| Junior secondary Basic 7-9) | 27 | 52.9 |
| Senior secondary(SS1 - SS3) | 24 | 47.1 |
| Do you address Mental health in the curriculum | | |
| Yes | 5 | 9.8 |
| No | 42 | 82.4 |
| No response | 4 | 7.8 |
| Work experience | | |
| less than a year | 3 | 5.9 |
| 1-3 years | 7 | 13.7 |
| 3-10 years | 5 | 9.8 |
| Over 10 years. | 36 | 70.6 |
| **C. Students** | | |
| Gender | | |
| Male | 522 | 74.9 |
| Female | 175 | 25.1 |
| Class | | |
| JSS1 - JSS3 | 275 | 39.5 |
| SS1 - SS3 | 422 | 60.5 |
| Do you learn about mental health | | |
| Yes | 218 | 33.4 |
| No | 435 | 66.6 |

Some items do not make up total of n= 1124 this is due to incomplete responses.

**Table 3.** Identified mental health problems in schools as perceived by stakeholders.

| Variable | n | % |
|---|---|---|
| **Depression** | | |
| Yes | 263 | 24.6 |
| No | 804 | 75.4 |
| **Aggression** | | |
| Yes | 561 | 52.7 |
| No | 504 | 47.3 |
| **Bullying** | | |
| Yes | 375 | 35.2 |
| No | 691 | 64.8 |
| **Drug abuse** | | |
| Yes | 98 | 9.2 |
| No | 971 | 90.8 |
| **Suicide attempts** | | |
| Yes | 125 | 11.9 |
| No | 926 | 87.1 |
| **Uexplained fear** | | |
| Yes | 340 | 32.6 |
| No | 702 | 67.4 |
| **Unexplained absenteeism** | | |
| Yes | 368 | 35.0 |
| No | 683 | 65.0 |

Some items do not make up total of 1124 due to incomplete responses.

knowledge of SMHS. Most of the students (67.2%), parents (59.0%) and teachers (72.5%) agreed on the need for SMHS in the schools they represented (Table 4)

Among the parents (96.8%) and the students (95.9%), the ideal referral place for children identified with mental health challenges was believed to be the hospital. While half of the teachers believed it was either the hospital or the school authorities respectively.

With regard to the ideal person who should be discussed with in the case of identifying a student with mental health problem, two hundred and ten (31.6%) of the students believed this should be the school principal, while 177 (26.7%) felt it should be with the parent of the student. Thirty nine (84.8%) of the teachers believed it should be discussed with a teacher; while parents felt it should be discussed with the school principal (47.2%) or the parents of the students (38.4%).

About 80.9% of students and 79.7% of parents believed that the ideal person to run SMHS should be a psychologist, while 86.0% teachers believed it should be by a teacher.

**Table 4.** Stakeholders experience and beliefs about SMHS.

| Experience / belief | Students (n = 697) | | Teachers (n = 51) | | Parents (n = 376) | | Total (n = 1124) | |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % |
| **Referral place for mental health challenges** | | | | | | | | |
| Hospital | 516 | 95.9 | 20 | 50.0 | 239 | 96.8 | 756 | 95.8 |
| School / staff | 11 | 2.0 | 20 | 50.0 | 6 | 2.4 | 19 | 2.4 |
| Others; church, non orthodox care | 11 | 2.0 | 0 | 0.0 | 2 | 0.8 | 13 | 1.6 |
| **Who to discuss troubled students with** | | | | | | | | |
| A teacher | 152 | 22.9 | 39 | 84.8 | 26 | 7.4 | 217 | 20.4 |
| School principal | 210 | 31.6 | 6 | 13.0 | 166 | 47.2 | 382 | 6.0 |
| Parent of the student | 177 | 26.7 | 0 | 0.0 | 135 | 38.4 | 312 | 29.4 |
| Others | 125 | 18.8 | 1 | 2.2 | 25 | 7.1 | 151 | 14.2 |
| **Willingness to be trained as counsellor** | | | | | | | | |
| Yes | 493 | 73.7 | 37 | 97.4 | 204 | 58.6 | 734 | 69.6 |
| No | 176 | 26.2 | 1 | 2.6 | 144 | 41.4 | 318 | 30.1 |
| **Ideal person to run SMHS** | | | | | | | | |
| Teacher | 96 | 14.5 | 37 | 86.0 | 56 | 15.6 | 186 | 17.8 |
| Psychologist/counsellor | 534 | 80.9 | 6 | 14.0 | 287 | 79.7 | 827 | 77.8 |
| Pastor/Islamic Imam/native healer | 14 | 2.1 | 0 | 0.0 | 11 | 3.1 | 25 | 2.3 |
| Not sure | 16 | 2.4 | 0 | 0.0 | 6 | 1.7 | 22 | 2.1 |
| **Mode for providing services for students** | | | | | | | | |
| Individually | 363 | 54.8 | 3 | 6.2 | 168 | 48.6 | 533 | 50.4 |
| Age groups | 73 | 11.0 | 13 | 27.1 | 48 | 13.9 | 134 | 12.7 |
| Class groups | 100 | 15.1 | 29 | 60.4 | 63 | 18.2 | 192 | 8.2 |
| Gender groups | 127 | 19.2 | 3 | 6.2 | 67 | 19.4 | 196 | 18.5 |
| **Where services should hold** | | | | | | | | |
| Within the school | 377 | 56.6 | 33 | 67.3 | 177 | 50.0 | 587 | 54.9 |
| At the district office | 31 | 4.7 | 6 | 12.2 | 13 | 3.7 | 50 | 4.7 |
| At the hospital | 96 | 14.4 | 3 | 6.1 | 55 | 15.5 | 154 | 14.4 |
| At the local health centres | 162 | 24.3 | 7 | 14.3 | 109 | 30.8 | 278 | 26.0 |
| **When should services be provided** | | | | | | | | |
| During school hours | 199 | 30.2 | 27 | 56.2 | 115 | 33.4 | 341 | 32.4 |
| After school hours | 177 | 26.8 | 2 | 4.2 | 90 | 25.12 | 267 | 25.4 |
| Weekends | 173 | 26.2 | 7 | 14.6 | 89 | 25.9 | 269 | 25.6 |
| Long holidays | 111 | 16.8 | 12 | 5.0 | 50 | 14.5 | 173 | 16.4 |
| **Should teachers have mental health education sessions?** | | | | | | | | |
| Yes | 551 | 82.4 | 46 | 95.8 | 268 | 77.7 | 863 | 81.3 |
| No | 117 | 17.5 | 2 | 4.2 | 77 | 22.3 | 196 | 18.5 |

Some items do not make up the exact total of 1124 due to incomplete responses.

Most of the respondents felt the services should either be provided on individual basis for students (50.4%) while others recommended that it should be according to gender groups (18.5%), class level (18.2%), or age groups (12.7%).

Over half recommended that the SMHS should be held within the school premises and not during the school hours (54.9 and 6.7%) respectively. Majority of the respondents in all 3 groups believed that both teachers and parents should have some mental health education training.

## DISCUSSION

Traditionally, child mental health services have been located within the community with children in need being referred outside of school for assistance. The provision of child and adolescent mental health services in schools have evolved in order to bring counselling and other mental health screening services onto the school site.

School mental health services present an avenue for early detection, and referral of mental health conditions among young persons. Most children in Nigerian schools do not have access to school mental health services. Key informants have been found to use derogatory terms in describing kinds of mental illness (Rondoni et al., 2010) and admit deficiencies in their training to deal with mental health problems.

Stigmatization of mental illness has also been found to be very prevalent among Nigerian school children (Jegede, 1978; Dogra et al., 2012). In our study, it was evident that the students felt there was a need for School Mental Health Services (SMHS) in their schools, with over 59% admitting to the perceived need for such a service within the school.

particularly in developing countries seems to play a role in determining their attitudes towards mental health issues and mental illness (Nastasi et al., 1998). Study in a South West Nigerian state found that teachers with higher levels of education showed less stigma and negative attitudes towards former mentally ill person (Aghukwa, 2009). In our study, though majority (70.6%) of the teachers had over 10 years working experience as teachers, only about a quarter of them had prior knowledge of school mental health services but more than half believed there was a need for such services in their school. The prior knowledge of school mental health services can be an indication of positive attitude towards SMHS. Some similar but larger international surveys have found different levels of awareness; from as low as 39% awareness of CAMHS among teachers (Kurtz et al., 1995), while in another as high as 80% level of awareness was found (Ford and Nikapota, 2000). Many teachers have been found by earlier researchers to be no better than the general public and school children in their understanding of mental health principles (Nastasi et al. 1998; Bryne 2001).

Stakeholders in this study could identify some behavioral problems among the students that they believed will benefit from mental health services. Some of the conditions reported in the schools were; bullying, unexplained absenteeism, aggression, depression, and suicide attempts. Aggression and unexplained absenteeism were the most commonly reported. Aggressive behaviour is often overt, very disturbing to school authorities and readily identified as potentially related to mental health challenges. However, unexplained absenteeism which is not attributed to ill health or legitimate absence due to unavoidable reasons or after obtaining permission may easily be overlooked. In reality such absenteeism may be early signs of truancy associated with conduct disorders and long term antisocial behaviour.

While it is useful that some of the stakeholders could readily identify certain traits in the students that may require mental health care, there is a need to further properly screen the students in order to identify at risk students, offer them care, while making effort not to see normal variations in students as problems. Caution is needed in such screening exercises to avoid misidentifying or stigmatizing such young persons.

Several useful suggestions were received from the stakeholders as pertains to what they perceive the services should entail as evident in this study. It is deemed necessary to engage stakeholders in the planning of such services as they often have their own views on how the services should be delivered. In this study location while parents and students felt mental health services should be provided by a psychologist the teachers generally believed it should be part of their own job. It is postulated that this finding may be due to a possible fear of being irrelevant if not involved in such practice. Failure to bear in mind such differences may result in the failure of laudable projects, especially if certain groups feel threatened.

Some researchers have suggested that there is a need for all stakeholders to participate in promoting wellbeing, resilience and protective factors (Adelman, 2006). Efforts are made at expanded school mental health work, to incorporate the input of stakeholders and their active participation (Nastasi et al., 1998, Adelman, 1995). The expanded school mental health projects are targeted at enhancing strategic collaborations to develop comprehensive systems that will strengthen students, families, schools and neighbourhoods and in doing so in ways that will maximize and enhance wellbeing.

A participatory intervention model is advocated to ensure a collaborative process in which the partners together create interventions to facilitate individual and cultural change, all focused in addressing the needs of students (Nastasi et al., 1998).

It was observed that many of the stakeholders (students, parents and teachers) were willing to be trained as counselors or mental health care providers within the school. This is similar in an earlier study among schools in South-Western Nigeria (Rondoni, 2009 ) where key informants

suggested that teachers are comfortable with handling mental health issues in children and they were willing to receive further training. The general willingness on the part of stakeholders in this study to volunteer and accept training in mental health, suggests a positive disposition towards collaboration. It has been recommended that the ideal mental health intervention in schools should make effort to create an atmosphere that fosters smooth transaction, provides informal encounters and social interactions, facilitates social support and provides opportunity for ready access to information and effective functioning (Adelman, 2006).

In our study, the respondents felt children identified to require mental health care should be discussed with the school authorities. Other researchers had also found that teachers would rather speak with parents or their colleagues than with child and adolescent mental health services (Ford and Nikapota, 2000).

In a study in the USA, that examined the kinds of mental health service provided in public schools (Teich et al., 2007), in almost all of the schools 96% reported at least one staff whose responsibilities includes providing mental health services to students. Three quarters had a school counsellor on staff, two thirds had a school psychologist or nurse and 44% had a social worker. In the schools in our study, only few respondents claimed to have a school psychologist in their schools. The willingness displayed by the respondents to be trained in being able to detect signs of mental health difficulty and volunteer in providing counselling after such training if a SMHS of started is noteworthy. This finding is similar to that reported by Ibeziako et al. (2008).

There is a need for combined creativity and energy of schools, public health and mental health professions (Adelman, 2006). Recommendations by stakeholders as to when and how the SMHS should run present areas for further focus group discussions, which can be useful in planning services that will be all inclusive.

A limitation of this study is the small sample of schools. The limited number of schools included in this study may not be fully representative of the entire state; as such these findings may not be generalisable to the larger population. In addition the recall of the respondents may be inaccurate of what exists in the schools but is used here to understand their perspectives. A more representative sample and detailed curriculum analysis will be employed in future effort.

## Conclusion

This study found that comprehensive school mental health services are lacking to these respondents representing the schools surveyed. It is obvious that there is a dire need for school mental health services in the study location. Different views exist about the extent and nature of such services. Stakeholders are willing to participate in the development and possible training as form of support for the SMHS establishment. There is a need for enlightening and engaging stakeholders in the planning cultural friendly services.

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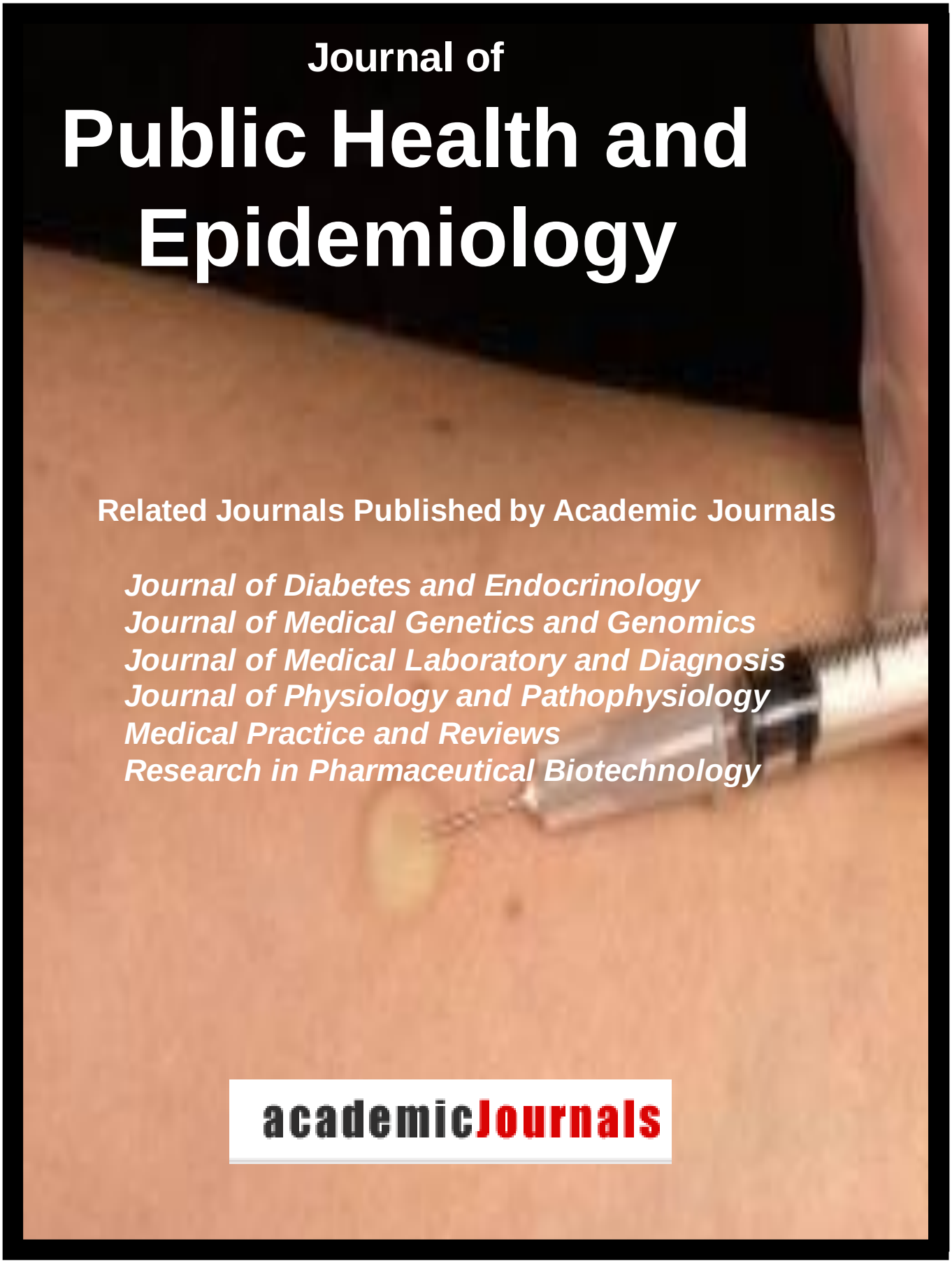

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